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Causes and Outcomes of Hospitalization among Systemic Lupus Erythematosus Patients in Aseer Central Hospital, Saudi Arabia: A Retrospective Study

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ABSTRACT

Objective: To identify frequency, causes and outcomes of hospitalisations among adult patients with systemic lupus erythematosus (SLE).

Methods: A record-based retrospective study was conducted at Aseer Central Hospital for a period of four and half years from January 2012 to June 2016. The study includes adult SLE patients who were diagnosed according to the 1997 SLE criteria.

Results: A total of 155 patients (8 males and 147 females) with 251 hospital admissions were included. The average admission rate for all cases was about 2.0 ± 1.0 times. The most commonly recorded causes of admissions were SLE nephritis flare (33.9%), and infections (16.3%). Mortality rate for SLE patients is almost 7.7% and the recorded main causes of death were pulmonary hemorrhage (33.3%), sepsis (25%), bilateral massive pulmonary oedema and pneumonia (8.3% for each).

Conclusion: Almost half of adult SLE patients are frequently hospitalized. Female patients and those with associated chronic co-morbidity have more frequent admissions. Consequences of SLE remain the most frequently recorded causes for hospital admission. Pulmonary complications are the main cause for death. Therefore, prompt and aggressive management of pulmonary consequences could markedly reduce disease mortality. Adopting preventive measures such as using prophylactic antibiotics and pneumococcal vaccination, early in the disease course, should be accentuated.

Keywords: Systemic lupus erythematosus, Hospitalization, Complications, Saudi Arabia, Retrospective study.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a worldwide autoimmune disorder with significant morbidity and mortality[1]. It is a persistent long-term disorder which is more common in women[2-3]. The underlying cause of autoimmune diseases is not fully understood, but the hidden process in SLE is that the immune system mistakenly attacks healthy tissues by using complexes or cytotoxic antibodies which impact on body organs[1,4]. Therefore, SLE has unevenness at onset that renders correct and early diagnosis quite challenging[5].

The concept of SLE has changed from being signed as a rare disease with increased mortality rate to a more known disease with benign consequences[6-9]. Morbidity from the disease remain high; the treatment outcome is highly variable, ranging from complete remission to death[10]. During the last few decades, there has been great improvement in SLE patients' survival, with more than 90% of SLE patients showing 5-year survival rate and 87.4% showing 10-year survival rate[11-12]. However, despite improvement of survival rate, mortality rate among SLE patients was estimated to be 4.6 times higher than general population[8].

Most SLE cases become hospitalised to receive treatment for disease manifestations, infections or associated medical health problems[13]. Several reports on hospital utilisation in SLE studied patients' characteristics associated with initial hospitalisation or predictors of mortality. Identifying both risk factors associated with early readmission and variation in readmission rates for SLE could potentially direct efforts to improve the quality of care during initial hospitalisations as well as during ambulatory care transitions[14-16].

It is essential to better understand the SLE-associated comorbidities that leads to frequent healthcare utilisation, such as emergency department visits and/or hospitalisation. Moreover, up to the best of our knowledge, there is no study that investigated causes of admission and outcome of hospitalisation of adult SLE patients in Aseer Region, Saudi Arabia. Therefore, there is a pressing need to investigate causes of admission and outcome of hospitalisation in our region, which will lead to improving the service provided to SLE patients.

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This retrospective study aimed to examine the causes and outcomes of hospitalization and healthcare utilization of patients with systemic lupus erythematosus.

METHODOLOGY

A record-based retrospective study was conducted by exploring all records of adult patients who were diagnosed as SLE and admitted to Aseer Central Hospital (ACH) – Aseer Region, Saudi Arabia, during the period from January 2012 until June 2016. A total of 155 adult patients were included, who fulfilled the 1997 SLE classification criteria[17], aged 12 years or more and have complete data on records. Patients' records were reviewed for patients' bio-demographic characteristics, disease duration since diagnosis was established based on the 1997 SLE criteria and all details regarding hospital admissions including number of hospital admissions, causes of each admission, length of hospital stay for each admission and the outcome on discharge (i.e., improved/ died). **The study was done after approval of ethical board of King Khalid university**.

Statistical analysis

After data were collected, it was revised, coded and fed to statistical software IBM SPSS version 21. The given graphs were constructed using Microsoft excel software.

All statistical analysis was done using two tailed tests and alpha error of 0.05. P value less than or equal to 0.05 was considered to be statistically significant. Descriptive statistics including frequencies and percent were used to describe the frequency of each category for categorical data. Mean with standard deviation and median with range was used to describe scale data according to shape of distribution. Chi square test / Mont Carlo exact test and Fishers exact test (if there were many small expected values) were used to test for association between patient hospitalization outcome and bio-demographic characteristics. For scale variables with skewed distribution, Mann-Whitney test was used to compare the variable descriptive between clinically improved and died patients. ANOVA and independent t-test were used to compare the rate of hospital admissions among the different sample characteristics.

RESULTS

A total number of 155 adult patients with 251 hospital admissions were included in this study. Table 1 shows the sample characteristics in relation to their admissions. Age of patients ranged from 13 to 78 years, with 8.4% aged below 20 years and 18.7% aged above 40 years. The majority of patients (95%) were females and 63.2% were married. Regarding duration of disease, 27.7% had the disease for 2 years or less, 39.4% had the disease for 3-4 years while 14.2% were diagnosed since more than 10 years. Eighty-four patients (54.2%) were free of any other health problems and the most frequently recorded co-morbidities were hypertension (23%), thyroid disorders (12%) and antiphospholipid syndrome (11%) (Figure 1).

Regarding the distribution of hospital admissions in relation to patients' characteristics, Table (1) shows that the overall admission rate was around two times and the highest admissions were recorded for those whose age was 40 years or more, compared to those who were below 20 years (1.97 vs. 1.54 times, respectively) (P= 0.097). The average number of admissions for females was higher than males (1.63 and 1.38) (P= 0.391), while the average of admission times for those who had the disease for more than 10 years was about 1.82 times which is higher than those who had the disease for 2 years or less (1.19 times) (P= 0.001). Patients with more than two chronic health problems were more admitted than others (2.1 times vs. 1.39 times, respectively) (P=0.001).

With regard to patients' admission data, table (2) shows that 54.8% of patients were admitted just once and 4.5% were admitted 4 to 5 times with an average number of admissions about two times. The average length of hospital-stay per each admission ranged from 1 to 144 days, with average length of 8 days. General wards were the setting of admission among 88% of cases. Regarding the cause of admission, 33.9% were admitted with SLE nephritis flare, 16.3% due to infection, 9.6% with SLE musculoskeletal flare and 8% due to venous thromboembolism (VTE). Other causes for admission were neuropsychiatric manifestations (6.4%), SLE mucocutaneous flare (6%), SLE hematological flare (4.8%), while other causes including musculoskeletal and mucocutaneous conditions were recorded among 2% of the patients. Considering the outcome of patients' admission, table (3) shows that 12 patients (7.7%) died and the recorded causes of death were pulmonary hemorrhage (33.3%), sepsis (25%), bilateral massive pulmonary oedema, and pneumonia (8.3% for each), autoimmune anemia, pancytopenia and chronic renal failure (8.3% for each). On relating outcome of patients' admissions with patients' characteristics to identify outcome determinants, table (4) shows that the average duration of disease was significantly longer among improved patients (6.7 ±5.0 years) than those who died (2.3 ± 2.2 years) (P=0.006). In addition, 15.4% of patients who were below 20 years old died compared to 3.4% of those who were 40 years or more (P=0.049). Regarding number of patients'

admissions, 10.6% of those who were admitted just once died compared to none of those who were admitted 4 times or more (P=0.008). About 31% of patients who were admitted for two weeks or more died compared to 1.4% of those who were admitted for one week or less (P<0.001).

Table (1): Bio-Demographic characteristics of patients with SLE in relation to hospital admission.

Bio-demographic data (n = 155)		No (%)	No of admissions			P
			Total	Range	Mean (SD)	
Age in years	< 20 years	13 (8.4%)	20	1-4	1.54 (0.96)	0.097
	20-	58 (37.4%)	89	1-4	1.53 (0.85)	
	30-	55 (35.5%)	85	1-3	1.55 (0.64)	
	40+	29 (18.7%)	57	1-5	1.97 (1.2)	
Gender	Male	8 (5.2%)	11	1-2	1.38 (0.21)	0.391
	Female	147 (94.8%)	240	1-5	1.63 (1.3)	
Marital Status	Married	98 (63.2%)	165	1-5	1.68 (0.96)	0.204
	Single	57 (36.8%)	86	1-4	1.51 (1.1)	
Duration since diagnosis (years)	1-2	43 (27.7%)	51	1-2	1.19 (0.25)	0.001*
	3-5	61 (39.4%)	114	1-5	1.87 (0.95)	
	6-10	29 (18.7%)	46	1-4	1.59 (1.6)	
	> 10	22 (14.2%)	40	1-3	1.82 (0.76)	
No. of Co-Morbidities	No	84 (54.2%)	117	1-4	1.39 (0.95)	0.001*
	One	42 (27.1%)	73	1-4	1.74 (0.76)	
	Two/ More	29 (18.7%)	61	1-5	2.10 (1.1)	

* P < 0.05 (significant)

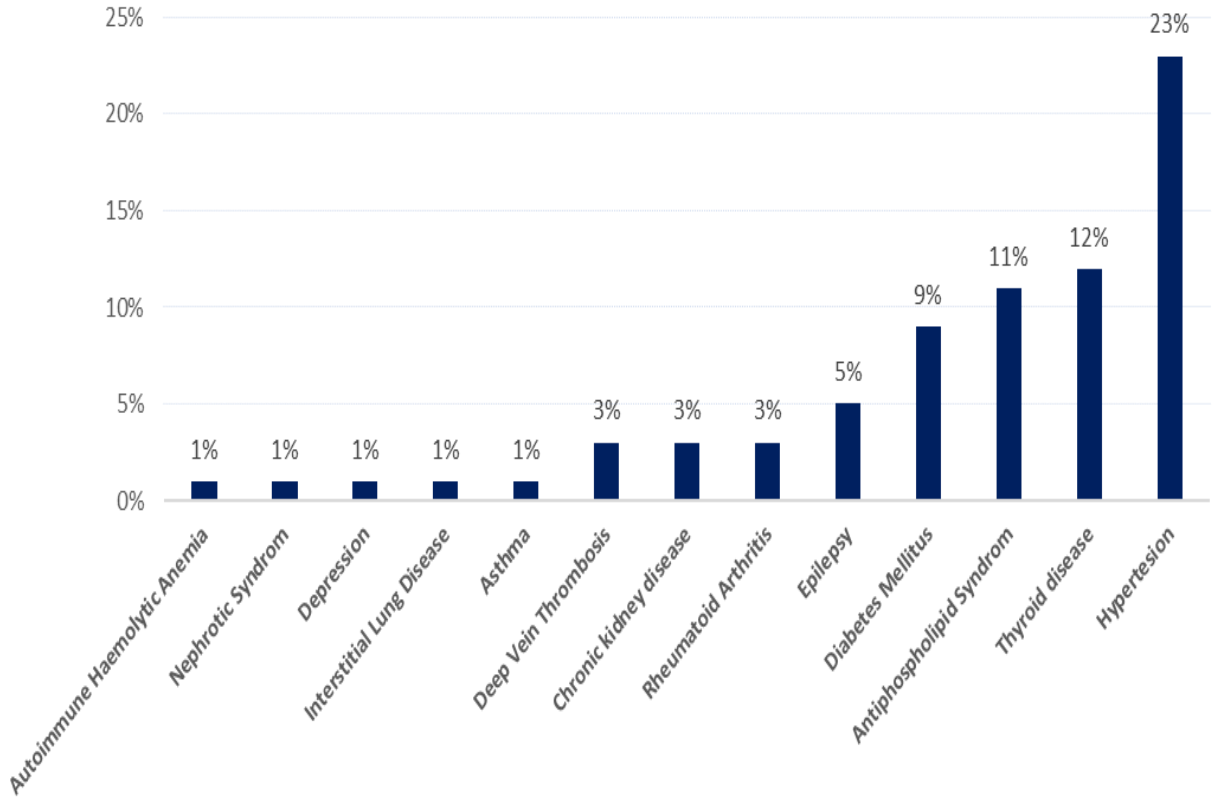

Figure 1: Health issues and co-morbidities recorded

Table (2): Characteristics of all hospital admissions

Patient admission data		No	%
Total number of patient admission (n=251)	One time	85	54.8%
	2-3	63	40.6%
	4-5	7	4.5%
Mean ± SD		1.9 ± 1.0	
Length of hospital stay / admission (days) (n=251)	1-7	114	45.4%
	8-14	79	31.5%
	15+	58	23.1%
Median (range)		8.0 (1-144)	
Department of admission (n=251)	General ward	221	88.0%
	Critical illness ward	30	12.0%
Cause of admission (n=251)	SLE Nephritis Flare	85	33.9%
	Infection	41	16.3%
	SLE Musculoskeletal Flare	24	9.6%
	VTE*	20	8.0%
	Neuro-Psychiatric Manifestation	16	6.4%
	SLE Flare Mucocutanous	15	6.0%
	SLE Flare Hematological	12	4.8%
	Nephritis other complications	14	5.6%
	Mucocutanous And Musculoskeletal	5	2.0%
	ACS**	4	1.6%
	Hematological and Musculoskeletal	3	1.2%
	Others	12	4.8%

*VTE: Venous thromboembolism**,** **ACS: Acute coronary syndrome

Table (3): Fate of admitted SLE patients

Fate of admitted cases		No	%
Outcome of hospitalized cases (n=155)	Improved	143	92.3%
	Died	12	7.7%
Causes of death (n=12)	Pulmonary hemorrhage	4	33.3%
	Sepsis	3	25.0%
	Bilateral massive pulmonary oedema	1	8.3%
	Pneumonia	1	8.3%
	Autoimmune Anemia (Active Hemolysis)	1	8.3%
	Pancytopenia	1	8.3%
	Chronic Renal Failure	1	8.3%

Table (4): Factors detecting fate of SLE patients

Factors		Outcomes				P
		Improved		Died		
		No	%	No	%	
Duration of disease (years)						
Range		1-25		1-7		
Mean ± SD		6.7 ± 5.0		2.3 ± 2.2		0.006#
Median		5.0		1.0		
Age in years	< 20 years	11	84.6	2	15.4	
	20-	55	94.8	3	5.2	0.049
	30-	49	89.1	6	10.9	
	40+	28	96.6	1	3.4	
Gender	Male Female	7	87.5	1	12.5	0.605
		136	92.5	11	7.5	
Diabetes Mellitus	Yes	13	92.9	1	7.1	0.930
	No	130	92.2	11	7.8	
Hypertension	Yes	34	97.1	1	2.9	0.219
	No	109	90.8	11	9.2	
Thyroid Disease	Yes	18	100.0	0	0.0	0.191
	No	125	91.2	12	8.8	
Ant phospholipid Syndrome	Yes	16	94.1	1	5.9	0.761
	No	127	92.0	11	8.0	
Total number of patient admission	One time	76	89.4	9	10.6	
	2-3	60	95.2	3	4.8	0.008
	4-5	7	100.0	0	0.0	
Length of hospital stays (days)	1-7	73	98.6	1	1.4	
	8-14	46	100.0	0	0.0	<0.001
	15+	24	68.6	11	31.4	

P: P-value
#: Mann-Whitney test

DISCUSSION

In this 4-years case series of 155 adult SLE patients, the average number of hospital admission was two admissions with 8 days for median length of hospital stay. The most commonly recorded causes of admissions were SLE nephritis flare (33.9%), infections (16.3%) or SLE musculoskeletal flare (9.6%). These findings are in accordance with those reported by several studies. Edwards *et al*. [18] noted that the cause of admission was clinical flare of SLE (58%), infection (37%) and thromboembolic disease (8%). **Rodríguez Montero *et al.*** [19], in Spain, reported an average of 3 times per SLE patient, over 17 years, with infections (25.5%) and clinical flare (16.6%) being the most common causes for hospitalisation. **Lee *et al.*** [3], in Canada, noted that most of SLE hospitalisations reported in literature were due to SLE flare (17.5%) and infections (16.2%). The mortality rate during the study period for SLE patients in our study was as high as 7.7%. Pulmonary hemorrhage and sepsis were the main causes for death (58.3%). However, lower rates were reported by **Rodríguez *et al.*** [19] (2%), Gu *et al*. [20] (2.8%), **Edwards *et al.*** [18] (3.2%) and **Doria *et al.*** [21] (4%). Sociodemographic disparities including race, ethnicity and geographic region were reported to influence SLE outcomes which could explain these variations in case fatality rates[22, 23].

On studying predictors of mortality, duration of disease, age, and length of hospital stay were the only significant predictors. As for duration of disease, it was clear that the higher mortality rate was recorded among recently diagnosed cases. (2.3 ± 2.2 years cut off point compare to 6.7 ±5.0 years for those who survived). This may be due to aggressive management with immunosuppressive agents. This aggressive management could increase the risk of sepsis which was recorded as one of the dominant cause of death in the current study (Table 3).

Significant predictors for admissions among SLE patients in our study were presence of associated comorbidities, age of less than 20 years and female gender. Moreover, significant predictors for mortality were young age (less than 20 years), less hospital admissions and prolonged hospital stay (more than 15 days). Moreover, Hernández-Cruz reported that variables associated with mortality among Mexican SLE patients included number of previous admissions and the number of severe infections[24]. Manger *et al*. reported that risk factors for death among SLE patients were male sex, age >40 at disease onset, associated comorbidity, e.g., heart disease, and central nervous system disease[25].

Edwards *et al*. [18] noted that deaths among SLE patients were mainly due to infection. The main predictors of death were previous multiple admissions, presence of infection and younger age. Feng *et al*. [26], in China, reported that the main risk factors associated with death among SLE patients were infection (30.1%), neuropsychiatric impairment (14.8%), renal failure (14.4%) and cardiopulmonary involvement (8.5%). Patients older than 45 years and with disease durations more than 2 years at admission had unfavorable short-term outcome.

Almost half of SLE patients in our study were hospitalised more than once. The median length of hospital stay was 8 days, and 12% of those hospitalised were admitted to the critical illness ward. Moreover, most of those who were hospitalised had associated comorbid conditions (e.g., hypertension in 23%, thyroid disease in 12%, diabetes in 9%,). These findings reflect poor disease control among SLE patients in our study.

These findings are in accordance with those reported by Feng *et al*., who noted that 12.6% of their SLE patients had comorbidities at the time of admission, where diabetes, infection and hypertension accounted for the most frequently associated non-autoimmune comorbidities[26]. In Tunisia, Jallouli *et al*. [5] reported that 28.7% of SLE patients were admitted twice or more, with a median length of stay of 11 days, with infections were one of the leading causes of hospitalisations (9.4%). Petri and Genovese reported that the average length of stay for SLE patients was 9.6 days[27].

Goldblatt *et al*. [28] noted that, despite the great improvement in the management of SLE, infection remains an important cause of morbidity and mortality in patients with SLE.

In conclusion, approximately half of SLE patients become frequently hospitalised. Female patients and those with associated chronic morbidity have more frequent admissions. Consequences of SLE (e.g., nephritis, infections and hematological flares) are the most frequently recorded causes for admission. Case fatality rate for SLE patients in our study was 2 times higher in comparison to other figures reported. Pulmonary hemorrhage and sepsis are the main causes for death. Therefore, prompt and aggressive management of pulmonary complications and infections could reduce disease mortality. Early in the disease course, preventive measures such as using prophylactic antibiotics and pneumococcal vaccination should be accentuated. This would improve care outcomes, minimise number of required hospital admissions, shorten hospital stay and therefore reduce the burden of disease.

Study Limitations

This study was a single center study; however this center is a central referral tertiary hospital which cover all Aseer region. The majority of cases all over the region are referred and managed in this central hospital. Therapy related data were not collected due to the observed varieties in types and doses used for immunosuppressive agents in each admission. In addition, due to lack of data, SLE disease activity score and damage index was not calculated.

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