Outcome of Systemic Lupus Erythematosus in Hospitalized Patients: A 2-year retrospective analysis

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Abstract: The objectives of the current study were to assess the pattern of hospital admissions among .Systemic lupus erythematosus SLE patients, to identify prognostic factors for survival, and causes of mortality among these patients. The current study involved a retrospective record review for all admitted SLE patients over 2 years (from April 2010 to April 2012), King Abdul Aziz University Hospital, Saudi Arabia, Jeddah. The results indicated that, a total of 95 admission episodes of 60 patients, belonging to different racial origins, were included 6 of the total patients sample [representing 6.3%] male and 89 [93.7%] female admissions; where the samples origins are as follows: Arabs 51 [53.7%], Blacks 28 [29.5%] and others 15 [4.3%]). Mean systemic lupus erythematosus disease activity index (SLEDAI) score was 11.56 (range 0-38). The mean duration of admission was 13.65 days (range 1-64), 48 admissions (50.5%) were due to active SLE and 47 (49.5%) due to other causes. Eleven patients (11.6%) were transferred to the intensive care unit (ICU). A total of 8 (8.4%) deaths were recorded. The results concluded that the renal disease continues to remain one of the most common serious organ involvements in SLE. Infection is a common cause of death among SLE patients. Thrombocytopenia and low hematocrit are independent risk factors for SLE related death. SLE related mortality is higher among the non-White and Black populations.
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1.Introduction:

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease affecting the skin, joints, kidneys, lungs, nervous system, serous membranes, and other organs of the body. The clinical course of SLE is variable and may be characterized by periods of remissions and of chronic or acute relapses. Women, especially in the age of twenties and thirties, are affected more frequently than men, (Von Feldt JM. 1995). The intensity of the clinical manifestations of SLE may vary among different groups of patients, which could range from mild rashes and arthritis to debilitating fever, fatigue, arthralgia; and to severe organ failure and life-threatening disease in worst cases, (Askanase, et al. 2012). The survival rates of SLE patients have significantly improved over the past 5 decades. However, as compared to the general population, a 3 to 5-fold increased risk of death, continues to persist, (Bongu et al., 2002).

The reported prevalence of SLE in the population is 20 to 140 cases per 100,000. (Chakravarty, et al. 2007). SLE is not a rare disease in Saudi Arabia with an estimated prevalence of 20 cases per 100,000. (Al-Arfaj, et al., 2002).

The 5-year survival rate in SLE has dramatically increased since the mid-20th century from approximately 40 percent in the 1950s, to more than 90 percent in studies conducted after 1980 (Trager, 2001). This trend has continued into the early 21st century (Urowitz, et al., 2008). However, poor survival in SLE is still reported in certain ethnic groups such as Indians (Kumar, et al., 1992), Black Caribbeans (Nossent, et al., 1993) and Hispanics (Lopez-acuna, et al., 1982).

The improvement in SLE can be attributed to a number of factors such as the early diagnosis of renal disease, better serological monitoring, more judicious use of corticosteroids and cytotoxic agents, availability and advancement of renal replacement therapy; and better management of associated complications like infection, hyperlipidemia and hypertension (Donadio, et al., 1995). Despite the overall improvement in the survival of SLE, 10-25% patients are yet known to die within 10 years of disease onset (Rubin, et al.,1985). The major cause of death in the first few years of illness is active disease manifested in the form of nervous, renal, or cardiovascular complications or infection due to immunosuppression; while late deaths are either caused by end-stage renal disease, treatment complications (including infection and coronary disease), non-Hodgkin lymphoma, and lung cancer (Rubin, et al.,1985; Abu-Shakra, et al., 1995 and Bernatsky, et al., 2006).

Previous studies had identified several prognostic factors for survival and found increased risk associated with the female sex, younger age, shorter SLE

duration, and Black/African American race (Bernatsky, et al., 2006). Older age, male sex, poverty, and a low complement may also be poor prognostic factors (Kasitanon, et al., 2006). Neuropsychiatric involvement, anemia, azotemia, cardiopulmonary involvement (Feng, et al., 2011), renal damage, thrombocytopenia, a SLEDAI score of less than or equal to 20 at presentation, lung involvement, and age less than or equal to 50 years at diagnosis; are prognostic factors associated with mortality (Abu-Shakra, et al., 1995). The objectives of the current study were to identification of the pattern of hospital admission of SLE patients, as well as, todetermining the prognostic factors for survival of SLE patients and also, to determining the causes of mortality among SLE patients.

2.Methods

The study was carried out retrospectively at King Abdul Aziz University's teaching hospital, Jeddah, Kingdom of Saudi Arabia. The records of all SLE patients admitted to the hospital, over a period of 2 years (between April 2010 and April 2012), were included in the study. The study was approved by the local ethics committee.

All patients included in the study fulfilled the American College of Rheumatology (ACR) criteria for SLE classification (Tan, et al.1982). The data obtained for each case of admission included in the study, comprised of; age, sex, race, admission source (emergency or elective), admission duration, cause, current SLE symptoms, immunosuppressive therapy received during admission, laboratory data and extent of disease activity determined using SLEDAI (Gladman, et al., 1994), admission outcome (discharge or death), and intensive care unit (ICU) transfer during admission.

Statistical analysis:

Statistical Product and Service Solutions (SPSS) package version 18 was used for conducting statistical analysis. Descriptive statistics was used for introducing the sample. After reaching normality, the independent t-test was used for comparing the mean values of treatment groups. Chi-square test was used for establishing the relationship between two variables. The study used 95% confidence interval and p-value<0.05 was considered as statistically significant.

3.Results:

A total of 95 admission episodes of 60 patients, belonging to different racial origins, were included 6 male admissions representing [6.3%] of the total samples and 89 [93.7%] female admissions; where the samples distributed according to their origin to arabs 51 [53.7%], blacks 28 [29.5%] and others 15 [4.3%]. Mean systemic lupus erythematosus disease activity index (SLEDAI) score was 11.56 (range 0-38). The mean duration of admission was 13.65 days (range 1-64), 48 admissions (50.5%) were due to active SLE and 47 (49.5%) due to other causes. Eleven patients (11.6%) were transferred to the intensive care unit (ICU). A total of 8 (8.4%) deaths were recorded. Descriptive data pertaining to study patients has been presented in Table 1.

Table 1: Descriptive data of study patients

Type	Minimum	Maximum	Mean	Standard Deviation
Age	14	62	30.38	12.470
Duration of Admission	1	64	13.65	12.984
WBC	.8000	27.4700	7.121914E0	4.9516909
Hb	3.4000	15.1000	9.416021E0	2.3196977
Platelet	1	662	239.12	131.993
Creatinine	36	1097	143.40	217.113
SLEDAI	0	38	11.56	8.226
dsDNA	14	2909	871.84	702.978

dsDNA double stranded deoxyribonucleic acid; Hb hemoglobin; SLEDAI systemic lupus erythematosus disease activity index

Patients' status with respect to sex, SLE mediated complications, and immunosuppressive therapy has been summarized in Table 2. A summary of the occurrence of SLE, in the study population with respect to demographic characteristics, systemic complications, type of hospitalization (emergency/elective), SLEDAI score, and status of immunosuppressive therapy has been presented in Table 3.

Analysis of SLE related deaths in the study population revealed that all cases of deaths were females. These deaths were most commonly reported among Arab women in the study population followed by Blacks. Infection was the most common cause of these deaths. Independent association was noted between mortality and thrombocytopenia. A summary of the causes of deaths that were reported in the study has been presented in Table 4.

Table 2: Patient characteristics on admission

Type	At admission n (%)
Male	6 (6.3%)
Female	89 (93.7%)
Emergency admission	73(78.5%)
Elective admission	20 (21.5%)
Rash	14(14.8%)
Fever	38(40 %)
Arthritis	14(14.8 %)
Renal impairment	21(22.1 %)
Proteinuria (>500 mg/24 hours)	12(12.6%)
Kidney biopsy during admission Class IV Class V	20(21 %) 7(7.4 %) 4(4.2 %)
Central Nervous System involvement	9(9.5 %)
Infection	20(21.1%)
Corticosteroid	92(96.8 %)
Cyclophosphamide	6(6.3 %)
Cellcept	17(17.9 %)
Azathioprine	14(14.7 %)
Hydroxychloroquine	80(84.2 %)

Table 3: Overall summary of study population

Variable	Admission no.
Sex	
Male Female	0 (0 %) 8 (100 %)
Admission source	
Emergency admission Elective admission	8 (100 %) 0 (0 %)
Race	
Arab Black Others	4 (50 %) 3 (37.5 %) 1 (12.5 %)
Systemic complications	
CNS involvement Renal impairment Proteinuria Infection Thrombocytopenia Anemia	2 (25%) 5 (62.5 %) 4 (50 %) 6 (75%) 5 (62.5 %) 8 (100 %)
Lupus nephritis	2 (25 %)
Class IV Class V	1 (12.5 %) 1 (12.5 %)
SLEDAI >20	2 (25%)
Immunosuppressive therapy	
Corticosteroid* Cyclophosphamide Cellcept	5 (62.5 %) 2 (25 %) 2 (25 %)

*high dose corticosteroid > 1mg/kg of prednisone or its equivalent or pulse methylprednisolone therapy

Table 4: Causes of deaths: Study population

Patient no.	**Age**	**Cause of death**
1	21	Pulmonary Tuberculosis, Multi organ dysfunction syndrome (renal failure, disseminated intravascular coagulopathy), gram negative sepsis
2	54	Convulsion, renal impairment
3	41	Gram negative sepsis, renal impairment
4	35	Renal impairment, lupus nephritis class IV
5	14	Renal impairment
6	39	Dead on arrival
7	14	Central nervous system involvement, lupus nephritis class IV, gram negative sepsis
8	26	Community acquired pneumonia, septic shock

4. Discussion and conclusions:

This was a retrospective study to identify the pattern of hospital admissions, prognostic factors for survival and causes of mortality among SLE patients.

The major cause of death in the first few years of illness is active disease manifested in the form of nervous, renal, or cardiovascular complications or infection due to immunosuppression; while late deaths are either caused by end-stage renal disease, treatment complications (including infection and coronary disease), non-Hodgkin lymphoma, and lung cancer (Rubin, et al.,1985; Abu-Shakra, et al., 1995 and Bernatsky, et al., 2006).

Infection was the most common cause of SLE related deaths in the study, followed by active SLE with severe organ involvement. These findings are consistent with those reported in other studies (19,20).

A number of lupus and non lupus related factors have been described in association with the prognosis of SLE (Abu-Shakra, et al., 1995 and Bernatsky, et al., 2006; Kasitanon, et al., 2006 and Feng, et al., 2011). Moreover, patients who died of active SLE are more likely to have CNS disease (Feng, et al., 2011), which was noted in the current study while analyzing mortality due to active SLE. Lupus nephritis, especially class IV, is clinically known to have a poor prognosis (Schwartz, et al., 1989). Similar findings were noted in the current study, in patients diagnosed with class IV lupus nephritis.

Hematological manifestation, especially thrombocytopenia, has been cited as an adverse factor deteriorating the prognosis of SLE (Abu-Shakra, et al.,

1995). A similar finding was reported in the current study wherein thrombocytopenia was noted to be an independent risk factor of SLE related mortality.

Race appears to play a role in disease prognosis in SLE, although it is difficult to separate the effect of socioeconomic status from the parameter of racial origin. SLE and its related mortality are known to have a notable predilection towards the Black population (Bernatsky, et al., and Mody, et al., 1994). This is consistent with the findings of the current study wherein patients belonging to the non-White and Black races were more seriously affected with SLE with a higher rate of mortality as compared to their non-Black counterparts in the study.

Age at onset of SLE has also been reported as significant predictor for survival (Bernatsky, et al., 2006). However it is noteworthy that different studies have presented conflicting results regarding the impact of the age at onset of SLE on the risk of SLE related mortality. Some studies have shown that SLE occurring at an advanced age escalates the risk for SLE related mortality (Abu-Shakra, et al., 1995 and Kasitanon, et al., 2006) whereas a few have concluded that late onset SLE runs more benign course (Font, et al., 1991 and Ho CTK, et al., 1998). Among the 8 deaths that were noted in the current study, 7 (87.5%) were among young patients while only 1 (12.5 %) death was reported in a patient above 50 years of age.

The effect of gender on SLE survival is also controversial. Previous studies have failed to show gender difference in damage and mortality rates of SLE (Miller, et al., 1983 and Mok, et al.,1999). One of the most notable findings of the current study was that all cases of SLE related deaths were females among the study population.

However, the current study did have a few methodological limitations related to study design and study sample. The study was retrospective in nature, included a relatively small sample size, was conducted at a single center and involved multiple racial and ethnic groups.

Renal disease continues to remain one of the most common serious organ involvements in SLE. Infection is a common cause of death among SLE patients. Thrombocytopenia and low hematocrit are independent risk factors for SLE related death. SLE related mortality is higher among the non-White and Black populations.

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