ORIGINAL ARTICLE

Mortality Patterns in Malaysian Systemic Lupus Erythematosus Patients

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Summary

A retrospective analysis of the case records of 494 systemic lupus erythematosus (SLE) patients under follow-up at University Hospital, Kuala Lumpur during 1976 - 1990 was performed. Overall mortality was 20.2% (100 patients). The causes of death were infection (30%), renal (15%), respiratory (14%), neurological (5%), cardiovascular (7%), other causes (2%) and unknown (27%). Active SLE was a contributing factor in 19% of the deaths. The patients who died had significantly more renal disease, neurological disease, serositis or thrombocytopenia by the end of the first year of disease compared to the survivors. As in other series, infection and active SLE remain important causes of death.

Key Words: Mortality, Systemic lupus erythematosus, Outcome, Prognosis

Introduction

Survival of patients with systemic lupus erythematosus (SLE) has improved significantly over the past 40 years[1]. With the advances in treatment options, early deaths from infection and active SLE are on the decrease and late deaths from complications of the disease or therapy are becoming more common[2]. Although SLE is a common disease in South East Asia, only a few studies previously have looked at mortality patterns[3,4,5,6]. We have previously reported on the clinical features in a cohort of SLE patients in Malaysia. The cumulative patient survival at 5 and 10 years was reported to be 82.3% and 70.5% respectively[7]. This article expands on the mortality data in this group of patients, looking at the causes of death and the clinical characteristics of the patients.

Materials and Methods

During the period 1976 to 1990, 494 patients were followed up longitudinally at our centre. All patients fulfilled the 1982 revised ARA criteria for the diagnosis of SLE[8]. A retrospective analysis of the case notes was performed to obtain the clinical data. Information on sex, race, age, age at disease onset, date of disease onset, duration of disease at presentation, date of death (if available), time of onset of clinical features according to ARA criteria, treatment modalities and cause of death. Active disease was recorded as present if there was a flare of SLE documented in the case notes just prior to death. The cause of death was obtained from the medical records or the death certificate, if available. It was defined as the primary event that led to the patient's demise. None of the patients had a post-mortem.

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Data entry was performed using DBase IV. Statistical tests used were the student's T-test and the chi-squared test. No corrections were made for multiple comparisons.

Results

There were 100 deaths (20.2%) during the 15 year follow-up period. The demographics of the patient groups are shown in Table I. There was no difference in the sex or race distribution, age at disease onset and duration of disease before presentation between the 2 groups. The mean age of death was 28.6 ± 11.1 (SD) years. The median duration of disease before death was 12.0 months (range 1 - 169 months). In those whose exact date of death was known, death occurred within 2 years of diagnosis of SLE in 74.7%.

The causes of death are shown in Table II. In 27 cases, we were informed by relatives/friends that the patients had died or their name was seen in an obituary in the newspaper. In these, no further details were available on their cause of death. The type of infection leading to death are as follows: septicaemia 11 (11%), pneumonia 4 (4%), *pneumocystis carnii* pneumonia 5 (5%), *pseudomonas aeroginosa* infections 2 (2%), fungal infections 2 (2%), meningitis 2 (2%), gram negative organisms 2 (2%), varicella pneumonitis 1 (1%) and gram positive organisms 1 (1%). Where the source of the pathogen was known, it came from the respiratory tract in 10 cases (33.3%), the central nervous system in 2 cases (6.7%) and the skin in 3 cases (10%). Patients with SLE who died ("toxic SLE") (19%) had multi-system involvement. The following were the main organ system involved: renal/lupus nephritis 12 (12%), and cerebral lupus, acute endocarditis, myocarditis, pneumonitis, pulmonary hypertension, pulmonary haemorrhage, thrombocytopenia, all 1 each (1%). There was no significant differences in the cause of death of those patients who died between 1976 - 1982 compared with those who died between 1983 - 1990.

Table I
Demographic Profiles of the Deceased and Survivors

	Deceased N = 100	Survivors N = 394
Chinese, n (%)	73 (73%)	377 (76.3%)
Malay, n (%)	18 (18%)	89 (18.0%)
Indian, n (%)	9 (9%)	27 (5.5%)
Other. n (%)	0	1 (0.2%)
Female:Male ratio	93:7	229:18
Mean age of disease onset (±S.D.)	24.8±10.4 years	25.8±9.85 years
Mean duration of disease before presentation (± S.D.)	24.0±37.53 months	18.6±30.0 months

Table II
Causes of Death in Malaysian SLE Patients 1976-1990

Cause	%
Infection	30
Renal disease	15
Respiratory disease	14
Cardiovascular disease	7
Neurological disease	5
Other causes*	2
Unknown	27

**Ovarian carcinoma 1, acute anaphylaxis 1*

The patients who died had significantly more renal disease (85% vs 69.5%, $p = 0.002$), neurological disease (30% vs 18.3%, $p = 0.01$), serositis (41% vs 16.2%, $p < 0.001$) and thrombocytopenia (34% vs 18.5%, $p < 0.001$) compared to the survivors (Table III).

Table III
Clinical Profiles of the Deceased and Survivors

Group Time Clinical Features Present	Deceased Overall (N=100) n (%)	Deceased First Year (N=100) n (%)	Survivors Overall (N=394) n (%)	Survivors First Year (N=394) n (%)
Arthritis	33 (33)	30 (30)	194 (49.2)	151 (38.4)
Neurological disease	36 (36)	30 (30)*	96 (24.4)	72 (18.3)*
Malar rash	73 (73)	67 (67)	315 (79.9)	285 (72.3)
Photosensitivity	40 (40)	32 (32)	188 (47.7)	152 (38.6)
Renal disease	94 (94)	85 (85)*	348 (88.3)	274 (69.5)
Serositis	47 (47)	41 (41)*	90 (22.8)	64 (16.2)*
Haematological disease	86 (86)	76 (76)	340 (86.3)	275 (69.8)
Neutropenia	43 (43)	34 (34)	168 (42.6)	119 (30.2)
Lymphopenia	76 (76)	65 (65)	321 (81.5)	237 (60.2)
Thrombocytopenia	48 (48)	34 (34)*	111 (28.2)	73 (18.5)*

** $p < 0.01$ between the survivors and the deceased*

Discussion

This study reports on the mortality data of the largest cohort of SLE patients in South East Asia. There were 100 deaths in our cohort of 494 patients followed up longitudinally over a period of 15 years. Other studies from this area have studied smaller groups over shorter periods of time and consequently had fewer deaths to analyse[3,4,5,6]. Results from our study concur with others from this region in that infection remains the most important cause of death in SLE patients, closely followed by active disease[4,5,6]. Our 5 and 10 year cumulative survival rate of 82.3 % and 70.5% respectively are much lower than previous studies[1,2] even when compared to studies looking at mortality rates in the 1970s[9]. We do not feel that this is due to the late presentation of patients to hospital as there was no difference in the mean duration of disease before presentation between the deceased and alive groups. However, 2 possible reasons for this may be, firstly, more severe infections are seen in our patients and secondly, the presence of more severe disease in our patients with multiple organ involvement at an earlier stage of their disease. As with other Oriental SLE populations, there was a high incidence of renal disease in our cohort[3,7] compared to Caucasian populations and the presence of renal disease has been shown to be associated with a poor prognosis[1,10].

In this study, the majority (74.7%) of patients died within 2 years of diagnosis of SLE. Therefore, unlike the previous published study of Malaysia[4] and studies of Caucasian populations[2], we are unable to show a bimodal pattern of mortality. It is likely that the patients in our study did not survive long enough to develop coronary artery disease, which was not among the recorded causes of death in this cohort. This is in keeping with other studies of Oriental SLE patients which have also not found coronary artery disease to be an important cause of death[5,6]. In addition, there was no difference in the causes of death in the period 1976 - 1982 compared to those who died between 1983 - 1990 which would suggest patients were not surviving long enough to develop the long-term complications.

One of the potential biases in this study is the relatively large number of "unknown" causes of death. Where a death occurred in hospital, attempts were made to obtain a copy of the death

certificate. However, many of these patients died outside hospital and often, we would only be informed of the death after a period of time. In these cases, no further medical information on the cause of death was possible. Thus, it may be entirely possible that we missed the late deaths due to cardiovascular disease, if they had all died outside hospital. However, other studies in Oriental SLE populations have not found an increased cardiovascular mortality[5,6] and it would be unusual for it to occur in isolation in our population. In addition, a recent study has suggested that these 'lost-to-follow-up' patients would not have a differential mortality rate[11]. So, it would be reasonable to assume that their causes of death would be similar to the rest of the study population.

In this study, the presence of renal disease, neurological disease, serositis or thrombocytopenia, especially within the first year of diagnosis of SLE was significantly more common in the deceased group compared to the survivors. Major organ manifestations, particularly renal and central nervous system disease[1,10] and haematological manifestations especially thrombocytopenia[10,12] have been previously shown to be markers of poor prognosis. Recently, studies have shown serositis/lung involvement to be poor prognostic factors also[10,12]. In studies on oriental SLE populations, the presence of thrombocytopenia[5,6] renal disease and cerebral lupus[4,5] has been shown to be associated with poor outcome but there have been no previous reports on serositis, as in our study.

In conclusion, in this cohort of Malaysian SLE patients, infection and active SLE remain the most common causes of death. The presence of renal disease, neurological disease, serositis or thrombocytopenia in the first year of disease suggests a poorer outcome.

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