ORIGINAL ARTICLE

Outcomes of Patients Newly-diagnosed with Systemic Lupus Erythematosus Managed in a Tertiary Training and Referral Hospital in the Philippines

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ABSTRACT

Objective. To determine the one-year outcomes of newly-diagnosed patients with systemic lupus erythematosus (SLE) in a tertiary government hospital in Manila, Philippines.

Methods. After ethics approval, we reviewed the medical records of a cohort of 44 newly-diagnosed SLE patients at 6- and 12-months post-diagnosis in 2018-2019. The outcomes of interest were: modified lupus low disease activity state as defined (mLLDAS), remission, hospitalization, 30-day readmission, organ damage, and mortality.

Results. The patients were predominantly young females (mean age of 29 ± 9.9 years). There was an average interval period of six months between onset of symptoms and diagnosis (6.4 ± 10.8 months). The most common manifestations were mucocutaneous (86.4%), hematologic (63.6%), musculoskeletal (61.4%), and renal disorder (47.7%). There was at least one positive serologic test in 88.7%. Five patients (11.4%) had comorbidity, usually hypertension (9.1%). The initial lupus treatment consisted of moderate to high doses of glucocorticoids and hydroxychloroquine. Patients with life-threatening or organ-threatening disease, usually nephritis, received cyclophosphamide, azathioprine, or mycophenolate mofetil. One patient received rituximab. Fewer patients with nephritis received cyclophosphamide infusions during the first six months compared to the later six months.

Most of the hospitalizations (34/36) occurred during the first six months and 22 of these were for diagnosis. Seven patients had more than one hospitalization and five (20%) had 30-day readmissions. mLLDAS was achieved by 15 (34.1%) and 30 (68.2%) patients at 6- and 12- months, respectively. Only one patient was in remission a year after diagnosis. Seven patients (15.9%) were assessed with organ damage, six (13.64%) of them at 6-months post-diagnosis. Organ damage was most commonly renal. Four (9.1%) patients died, all during their initial hospitalization.

Conclusion. In our population observed over a period of one year (2018-2019), there was a very low rate of remission (1/44, 2.3%), mLLDAS in 68.2%, and organ damage in 15.9%. Most of the hospitalizations (65%) were for the diagnosis of lupus and all deaths (9.1%) occurred during this first hospital confinement. We must intensify our efforts to (1) achieve earlier diagnosis, (2) deliver optimal lupus treatment and supportive care during the first lupus hospitalization, and (3) initiate early and persistent immunosuppressive treatment for nephritis to improve outcomes for our patents with SLE.

Keywords: systemic lupus erythematosus, outcomes, remission, disease activity, hospitalization, organ damage, Philippines

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystemic autoimmune disease that has a wide variety and severity of clinical presentations. More severe manifestations are associated with frequent disease flares, more organ damage, higher health-care costs, and poor quality of life. The goals in the management of SLE include long-term patient survival, prevention of organ damage, and optimization of health-related quality of life. The 2019 EULAR clinical practice guideline states that treatment aims are remission or low disease activity state (LLDAS) and prevention of flares.[1,2]

Improvements in medical care of lupus have led to improved patient survival in recent years.[3] Latest treatment strategies include use of pulses of intravenous methylprednisolone and appropriate initiation of immunomodulatory/immunosuppressive agents to (a) hasten tapering or discontinuation of glucocorticoids, (b) manage organ/life-threatening cases, and (c) serve as 'rescue' therapy for non-responders. Biologic drugs are also recommended for refractory cases or for patients with intolerance or contraindications to standard immunosuppressive agents. Close monitoring of patients, assessment of treatment adherence, and disease control optimization are recommended to reduce flares.[4] Monitoring of disease activity is facilitated through the use of indices like the SLE Disease Activity Index (SLEDAI). However, access to and availability of laboratory tests is not always assured in low-resource settings like the Philippines. In the Philippine General Hospital (PGH), the most commonly used tool is the Mexican SLEDAI (MEX SLEDAI) wherein immunologic tests, that are quite costly, are omitted.

A retrospective study in Italy, with a seven-year follow-up (2010-2017), reports LLDAS in 87.8% and, among them, 96.5% satisfied the definition of remission. Longer periods of low disease activity led to decreasing proportion of patients with damage accrual. The increase in mean SLICC/ACR Damage Index (SDI), a measure of permanent organ damage in SLE, was found to be lower among patients in LLDAS for a minimum of two consecutive years.[2] Attainment of LLDAS has also shown to be associated with better quality of life.[4]

We hope to achieve a similarly high rate of low disease activity and remission among our service patients at the PGH. The PGH is one of the largest hospitals in the National Capital Region of the Philippines serving more than 600,000 patients annually.[5] It is one of the few hospitals in the country with a dedicated weekly Lupus Clinic serving an average 50 patients/week, the majority of whom are indigent. In addition, the Rheumatology Division attends to a weekly average of two patients with newly-diagnosed lupus. Increased awareness about lupus in the general population and among health practitioners will likely lead to earlier diagnosis and, hopefully, increase allocated resources for patient care to achieve better outcomes among lupus patients in our local population. This study aims to determine the achievement of remission or modified low lupus disease activity state in a cohort of newly-diagnosed SLE patients on the first year of follow-up in PGH. It also aims to determine other outcomes such as rates of hospitalization, 30-day readmission, organ damage, and mortality during this time period.

METHODS

Patients who were ≥18 years of age, newly diagnosed with SLE from January 2018 to July 2019 at the service wards and out-patient rheumatology clinic of the University of the Philippines-Philippine General Hospital (UP-PGH), and with known outcomes at 6- and 12-months post-diagnosis were included in the study. A patient was classified to have SLE based on the 1997 update of the 1982 American College of Rheumatology (ACR) revised criteria[6] or the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE[7]. Data collection was performed through chart review. Data on demographic characteristics, comorbidities, medication history, clinical and laboratory features, as well as medical management and outcomes at 6- and 12-months after diagnosis, were recorded.

Remission was defined as a MEX-SLEDAI score of 0 without glucocorticoid medication, while maintained on hydroxychloroquine as lupus treatment.[8] The lupus low disease activity state is conventionally defined with five conditions: (1) SLE Disease Activity Index (SLEDAI)-2K ≤4, with no activity in major organ systems [renal, central nervous system (CNS), cardiopulmonary, vasculitis, fever] and no haemolytic anaemia or gastrointestinal activity; (2) no new lupus disease activity compared with the previous assessment; (3) a Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLEDAI physician global assessment (scale 0– 3) ≤1; (4) a current prednisolone (or equivalent) dose ≤7.5 mg daily; and (5) well tolerated standard maintenance doses of immunosuppressive drugs and approved biological agents.[9]

However, given that the study was retrospective and immunologic tests (serum complement, anti dsDNA) were usually not done due to their cost, we used a modified definition of the lupus low disease activity state (mLLDAS) specific for this study as follows: MEX-SLEDAI score ≤3 while on hydroxychloroquine alone, or a MEX-SLEDAI score ≤4 while receiving hydroxychloroquine, prednisone equivalent dose ≤ 7.5 mg/day, and immunosuppressants in stable doses. Furthermore, glucocorticoid dose is defined according to the prednisone equivalents per day. Low dose refers to prednisone equivalent <7.5 mg/day, medium dose is >7.5 mg but ≤30 mg/day and high dose is 31-100 mg/day.[10] Descriptive statistics such as mean and standard deviation were used to present continuous variables and frequency and percentage for categorical data.

Ethical approval was obtained from the UP-Manila Research Ethics Board (UPM-REB Code: 2020-259-01) and the Expanded Hospital Research Office (EHRO) prior

to study initiation. The need for patient consent was waived because the study was retrospective. To protect patients' privacy, patient identifiers were removed and all data were recorded in a password-protected file accessible only to the principal investigators.

RESULTS

Study Population

A total of 165 unique new patients were gathered from a review of the 2018-2019 patient census database. We excluded 121 records because of the following reasons: year of diagnosis was prior to 2018 (n=66), incomplete records (n=21), the diagnosis was not SLE (n=18), and lost to follow up (n=16).

The study population (Table 1) consisted of 44 patients with incident SLE, 95.5% were females with 21:1 female to male ratio. The mean age was 29.0 ± 9.9 and 93.2% were unemployed. The majority of the patients came from the National Capital Region (59.1%) and Luzon (36.4%). Equal proportions of patients were diagnosed in the out-patient clinic and in-patient wards. The mean interval from onset of initial symptoms to diagnosis was 6.4 ± 10.8 months; 9.9 months among out-patients and 2.9 months among those hospitalized.

The initial disease activity score for 77.3% was a MEX-SLEDAI greater than 5 (active disease) and the rest had a score of 2-5 (possible active disease). The patients who were initially hospitalized had higher disease activity scores than those diagnosed in the outpatient clinic, with average scores of 13.9 and 7.4, respectively. The most common clinical manifestations (Table 2) were mucocutaneous disease (86.4%), followed by hematologic (63.6%) and musculoskeletal involvement (61.4%), then by renal disorder (47.7%). Two (4.5%) patients presented with life-threatening thrombocytopenia. There were 88.7% who had at least one positive serologic test: 28 (63.6%) were positive for anti-nuclear antibodies (ANA), 24 (54.5%) for direct Coombs test in the absence of hemolytic anemia, 23 (52.3%) for anti-double stranded DNA (anti-DsDNA), and 20 (45.5%) had low C3 levels. Only five patients (11.4%) had comorbidity at the time of diagnosis, four of whom had hypertension (9.1%).

Table 1. Demographic Characteristics of Newly-diagnosed Patients with SLE (n=44)

Characteristics	Frequency (%)
Female	42 (95.5%)
***Age** (years), mean ± SD*	29 ± 9.9
Employment status	
Employed/self-employed	3 (6.8%)
Unemployed	41 (93.2%)
Location of residence	
National Capital Region	26 (59.1%)
Luzon	16 (36.4%)
Visayas	1 (2.3%)
Mindanao	1 (2.3%)

Table 2. Clinical Characteristics of Newly-diagnosed Patients with SLE (n=44)

Characteristics	Frequency (%)
***Interval from initial symptom to diagnosis** (months), mean ± SD*	6.4 ± 10.8
Comorbidities	5 (11.4%)
Hypertension	4 (9.1%)
Diabetes	1 (2.3%)
Where diagnosed	
Out-patient clinic	22 (50.0%)
Charity ward	22 (50.0%)
MEX-SLEDAI score on diagnosis	
<2	0
2-5	10 (22.7%)
>5	34 (77.3%)
Manifestations/organ system involvement	
Non-specific manifestations	41 (93.2%)
Mucocutaneous	38 (86.4%)
Hematologic	28 (63.6%)
Musculoskeletal	27 (61.4%)
Renal	21 (47.7%)
Pulmonary	5 (11.4%)
Cardiac	4 (9.1%)
Neuropsychiatric	4 (9.1%)
At least one positive serologic test	39 (88.7%)

Medical Management on Diagnosis

At the initial medical encounter, all patients were given medium (n=10, 22.7%) or high-dose (n=34, 77.3%) corticosteroid therapy. Twelve patients (27.3%) received methylprednisolone pulse therapy (MPPT) with a mean total dose of 2083.3 ± 821.2 mg. The most common indications for MPPT were renal, hematologic, and neuropsychiatric manifestations (Table 3).

Forty-two (95.5%) patients were started on hydroxychloroquine (HCQ) at 200 mg/day (Table 3). Two patients were not prescribed HCQ for unknown reasons. Six (13.6%) patients with life- or organ-threatening disease were given additional immunosuppressive drugs. Among five patients with nephritis, two (4.6%) received intravenous cyclophosphamide (IVC) infusion, two got azathioprine 100 mg/day, and one had mycophenolate mofetil (Table 3). One patient (2.3%) received 500 mg of rituximab for hemolytic anemia and thrombocytopenia.

Management and outcomes at months 0-6

At the 6th month of follow-up, most of the patients were maintained on medium-dose (53.8%) or low-dose (33.3%) corticosteroid. Five (12.8%) patients were receiving high-dose corticosteroid for lupus nephritis flare (MPPT with an average total dose of 1500 mg). One patient who achieved mLLDAS had already discontinued cortico-

Table 3. Medical Management during the First Year of Newly-diagnosed Patients with SLE (n=44)

Medication	Number of patients		
	Initial	6th month	12th month
Prednisone			
Dose per day, mean ± SD	43.9 ± 16.2	16.2 ± 13.2	9.6 ± 10.7
Dose range	44 (100.0%)	39 (88.6%)	38 (86.4%)
<7.5 mg	0	13 (33.3%)	19 (50.0%)
7.5-30 mg	10 (22.7%)	21 (53.8%)	15 (39.5%)
31-100 mg	34 (77.3%)	5 (12.8%)	4 (10.5%)
Hydroxychloroquine, *200 mg/day*	42 (95.5%)	38 (86.4%)	38 (86.4%)
Methylprednisolone pulse therapy	12 (27.3%)	5 (11.4%)	1 (2.3%)
Total dose (mg), mean ± SD	2083.3 ± 821.2	1500	1500
Indication			
NPSLE	3 (25.0%)	2 (40.0%)	-
Hematologic	4 (33.3%)	1 (20.0%)	-
Renal	9 (75.0%)	4 (80.0%)	1 (100.0%)
Cardiac	3 (25.0%)	-	-
Others	1 (8.3%)	-	-
Intravenous Cyclophosphamide *(for nephritis)*	2 (4.6%)	12 (27.3%)	8 (18.2%)
Azathioprine 100 mg/day *(for nephritis)*	2 (4.6%)	1 (2.3%)	1 (2.3%)
Rituximab 500 mg dose *(for hemolytic anemia & thrombocytopenia)*	1 (2.3%)	0	0

Table 4. Outcomes at 6- and 12-months Post-diagnosis (n=44)

	Number of patients	
	6th month	12th month
Remission	0	1 (2.3%)
Modified low lupus disease activity state	15 (34.1%)	30 (68.2%)
Organ damage*	6 (13.6%)	7 (15.9%)
Average SDI Score, mean ± SD	1.2 + 0.9	1.8 + 0.8
SDI SCORE per organ		
NPSLE score of 1-3 points	1 (16.7%)	1 (14.39%)
Renal score of 1-2 points	2 (66.7%)	2 (66.7%)
Renal score of 3 points	1 (33.3%)	1 (33.3%)
Musculoskeletal score of 1-3 points	0	1 (14.3%)
Skin score of 1-2	1 (16.7%)	1 (14.3%)
Diabetes	1 (16.7%)	1 (14.3%)
Cumulative hospitalizations	34 (25)**	2 (2)**
Hospitalizations post-diagnosis	12	2
Readmissions	7 (7)**	0
30-day readmissions	5 (5)**	0
Deaths	4	0

* *There was no damage in the following organs: ocular, pulmonary, cardiovascular, peripheral vascular, gastrointestinal, premature gonadal failure, malignancy.*

** *The number in parentheses refers to the number of patients hospitalized.*

steroid medication and was maintained on hydroxychloroquine monotherapy. Two patients were non-adherent to hydroxychloroquine but had controlled disease activity with prednisone alone. Twelve patients (27.3%) were receiving IVC for nephritis; one was shifted from mycophenolate mofetil due to poor adherence. Two started IVC induction upon diagnosis while nine had later treatment induction (Table 3). Eight of ten patients whose IVC induction was initiated months post-diagnosis already had nephritis on diagnosis. The reason/s for the delay in IVC induction was not documented. Aside from IVC and azathioprine, that was maintained by one patient, there were no other immunosuppressive drugs in the treatment armamentarium at the 6th month of follow-up.

None of the patients achieved remission but fifteen (34.1%) achieved mLLDAS. Six (13.6%) patients were found to have organ damage with an average SDI score of 1.2 ± 0.9. Most of the organ damage was renal and one patient each developed diabetes, skin ulceration, and cerebrovascular accident (Table 4). There were 34 hospitalizations for 25 patients during the first six months, 22 (65%) were the initial medical encounter during which the diagnosis of SLE was known. Seven patients (28%) were admitted more than once and five patients (20%) had 30-day readmissions. The readmission rate was 20.5% (7/34) and the 30-day readmission rate was 14.7% (5/34). Four (9.09%) patients died, all during their initial hospitalization.

Management and outcomes at months 7-12

At the 12th month of follow-up, most of the patients were either on low-dose (n=19) or medium-dose (n=15) oral corticosteroids. Four patients were receiving high-dose corticosteroid, including one who received MPPT for nephritis. There were 38 patients maintained on HCQ, one on azathioprine, and one patient was newly started on mycophenolate mofetil for nephritis. Eight patients (18.2%) continued to receive IVC; one of them was maintained on a 12-month course from the time of diagnosis (Table 3).

By the 12th month post-diagnosis, one patient had achieved remission and the number of patients on mLLDAS had doubled (n=30, 68.2%). Our patient who achieved remission presented with cutaneous and renal manifestations (MEX-SLEDAI 8) in the out-patient clinic and was initially prescribed a medium dose of steroid and hydroxychloroquine on diagnosis. She had one hospitalization for lupus nephritis and had organ damage of diabetes and avascular necrosis attributed to corticosteroid use.

Seven patients (15.9%) had organ damage, mostly renal, and the average SDI score was 1.8 + 0.8. There were two (4.5%) hospitalizations, no 30-day readmissions and no mortalities (Table 4).

DISCUSSION

This study investigated the one-year outcomes of a cohort of 44 newly-diagnosed patients with lupus in one of the largest tertiary referral hospitals in the Philippines. Their demographic characteristics are similar to previously published data among Filipinos.[11,12] In our cohort, the interval from symptom onset to diagnosis was longer in the outpatient setting compared to those who were hospitalized. Lupus may present with non-specific and milder manifestations that patients may initially ignore and lead to a delay in seeking a formal consultation or may not readily be recognized as due to lupus. In the outpatient setting, there may be less urgency in performing tests or limited access to laboratory procedures due to unavailability or cost.

The most common lupus manifestations were similar to previous local studies. Skin manifestations were more common than musculoskeletal, hematologic, and renal.[11,12] However, renal involvement was the most common cause of permanent organ damage. Although the majority of the patients had at least one positive serologic test, not everyone underwent testing for all autoantibodies hence the results may show an underestimate.

Knowing the increased risk of cardiovascular disease in SLE, screening for and treatment of these comorbidities is almost as important as lupus disease control in newly-diagnosed patients. In our cohort, only a minority (11.4%) had comorbidities at baseline and these were seen among older patients (median age of 40 years), mostly hypertension (9.1%) and one (2.1%) had diabetes. A cohort of Koreans with lupus nephritis had a similar rate of incident HPN at 11.2% (36/322) but another cohort of 113 biopsy-proven lupus nephritis in Singapore had higher rates of HPN (21.2%) and diabetes mellitus (4.4%) than our study.[13,14] Moreover, analysis of registry data comparing a Danish lupus cohort (n=3,010) with 57,046 age-and sex-matched controls showed that most comorbidities studied were more than twice as prevalent in SLE patients versus the general population comparators.[15] The most common comorbidities (prevalence >5%) on SLE diagnosis were hypertension (24.0%), chronic pulmonary disease (7.8%), neuropathy (6.9%), depression (6.8%), cerebrovascular disease (6.6%), ocular disease (5.8%), cardiac arrhythmia (5.7%), coagulopathy (5.7%), and osteoporosis (5.6%).[15] A study of 1605 incident cases of SLE and 6284 matched controls from the UK primary care database established that on diagnosis of SLE, the risk of having a comorbidity was at least double for cancer, cardiovascular, renal, liver, rheumatological and neurological diseases as well as depression, anemia and psoriasis. Following diagnosis, patients with SLE also had higher risk of developing neoplasm, cardiovascular, genitourinary, metabolic/endocrine, gastrointestinal and hepatic diseases, chronic pulmonary diseases, musculoskeletal /connective tissue and neurological diseases.[16] In Taiwan, a population-based case–control study from the National Health Insurance Research Database (2010-2013) included newly-diagnosed SLE and matching controls. Diffuse diseases of connective tissue, followed by herpes zoster, were the comorbidities with the most significant positive association with incident SLE while diabetes mellitus was one of the diseases that had a significant negative association.[17]

Glucocorticoids are known to provide rapid relief of signs and symptoms of lupus thus all patients were treated with moderate to high doses after diagnosis, less than a third needed high-dose intravenous pulses. As recommended by treatment guidelines, glucocorticoid dose was tapered in all patients and was discontinued in two patients in our cohort. There were a few patients with disease flares (vasculitis or nephritis) whose steroid doses had to be increased on the 6th month (n=6) and on the 12th month follow-up (n=4). Most patients were maintained on a combination of a corticosteroid and another lupus control medication. Only two patients had corticosteroid monotherapy as initial treatment, and one of them continued the monotherapy until the 12th month. These two patients were maintained on a low-dose of steroid at the 12th month and had a MEX-SLEDAI score of 0 at 6- and 12-months post-diagnosis, without any hospitalization. This result is contrary to the study of Kan et al. (wherein patients who received corticosteroid monotherapy had poorer clinical outcomes.[18]

The latest treatment guidelines recommend the use of hydroxychloroquine for all patients with lupus, and the majority of our patients received it.[4] Other immunosuppressive drugs such as azathioprine, mycophenolate mofetil, and IVC were used among our patients with lupus nephritis. In comparison to cyclophosphamide, there were very few who were able to adhere to the other two drugs because of their higher cost.

Our study showed a very low remission rate, 0 at 6 months and 2.3% at 12 months. The one patient in remission at 12-months post-diagnosis, however, had organ damage from diabetes and avascular hip necrosis that adversely affected her overall quality of life. The proportion of mLLDAS increased from 34.1% at 6 months to 68.2% at 12 months. In comparison, a retrospective cohort of 116 newly-diagnosed SLE patients in Italy had a remission rate of 21.6% and 31.9%

at 6- and 18-months, respectively. LLDAS at 6-months was achieved by 42.2% and 46.6% at 18months. They found that achievement of LLDAS only was associated with a higher baseline disease activity score.[19] Another group of 769 SLE patients studied in Hong Kong for five years had complete remission in 280 (36.4%) patients at the last visit. Patients who remitted for ≥5 years were older, and had significantly lower prevalence of renal involvement, leucopenia, or thrombocytopaenia.[20] A cohort in China composed of 185 patients with early SLE [median (range) disease duration of 2.3 (0.8–7.7) years] was followed for a median duration of 2.2 (1.0–2.9) years. About a third of their patients (n=58, 31.4%) fulfilled LLDAS at recruitment, 81 (43.8%) patients achieved LLDAS during follow-up, and a quarter (n=45, 24.3%) never achieved LLDAS. Most of their patients (n=139, 75.1%) achieved LLDAS at least once. There were varying degrees of maintaining LLDAS: 29 (15.7%) patients were in LLDAS for 100% of observations, 53 (28.7%) for 50 to 100% of observations, and 58 (31.4%) in LLDAS for < 50% of observations.[21] Lastly, in a longitudinal collaborative study in nine countries in the Asia-Pacific region, 1846 patients were assessed and the criteria for LLDAS were met by 44%. There was low likelihood of LLDAS in patients with shorter disease duration (OR 0.31, 95 % CI 0.19–0.49), history of discoid rash (OR 0.66, 95 % CI 0.49–0.89), renal disease (OR 0.60, 95 % CI 0.48–0.75), elevated double stranded DNA (OR 0.65, 95 % CI 0.53–0.81) or low complement (OR 0.52, 95 % CI 0.40–0.67). Higher national social wealth of countries (OR 1.57, 95 % CI 1.25–1.98) as measured by the gross domestic product per capita was positively associated with LLDAS, but ethnicity was not.[22] Moreover, an earlier study has also demonstrated that personal socioeconomic status contributes to disease activity.[23]

Recent studies have demonstrated the relationship between LLDAS and organ damage. In the Italian cohort, there was less organ damage at 18 months among those in LLDAS or remission at 6 months. No one who achieved remission at 6 months and maintained it until 18 months had organ damage compared to >30% with organ damage among those who were not able to achieve or maintain remission.[19] In the Chinese cohort, damage accrual (increase in SDI by 1 or more) was observed in 21/141 (14.9%) patients within one year, which was similar to our data. They found increasing proportion with organ damage within two years (37/104 or 35.6%) and three years (11/21, 52.4%).[21] A prospective study of a multiracial group of 350 patients in the UK since 1991 showed an incidence of damage accrual at two years post-diagnosis of 39.6/1000 patient-years, and incidence of serious organ damage (SDI score ≥3) of 10.4/1000 patient-years.[24]

Furthermore, being able to maintain LLDAS was similarly associated with less organ damage accrual in a cohort of 293 Caucasians observed over seven years. LLDAS lasting 1, 2, 3, 4 or ≥5 consecutive years was achieved by 33 (11.3%), 43 (14.7%), 39 (13.3%), 31 (10.6%) and 109 (37.2%) patients, respectively. About 84% of their patients in LLDAS also fulfilled the criteria for remission. Patients who maintained LLDAS for at least two consecutive years had significantly less organ damage accrual compared with patients never in LLDAS (p=0.001).[2]

Our study showed that most with organ damage acquired it during the first six months after diagnosis, mostly from uncontrolled nephritis. There was only one additional patient with organ damage on the second half of the 1-year observation period. This emphasizes the importance of early aggressive treatment, especially for those with lupus nephritis, to achieve good disease control and prevent damage. Unfortunately, this is not always feasible because the medicines are costly and the oral long-term medications (azathioprine, mycophenolate mofetil, hydroxychloroquine, prednisone) are paid out of pocket since they are not covered by the national insurance (Philhealth). This is an area of healthcare delivery that must be improved through government subsidy or insurance reimbursement.

In addition, other studies have shown that the benefits of achieving LLDAS or disease remission include decreased risk of hospitalization and better health-related quality of life.[1,2,25] Among 453 patients who had QOL assessment, remission for ≥5 years was associated with significantly higher SF36 and the total health-related scores of the LupusPRO.[20]

Half of our patient cohort was diagnosed with lupus during an in-hospital admission but subsequent readmission rates were lower. Both patients who had hospitalizations 7-12months from diagnosis had nephritis. One of them had persistently high disease scores and was hospitalized four times during the 12-month period from diagnosis. Of the five patients who were readmitted within 30-days from prior hospitalization, only one was related to lupus activity (NPSLE); two were due to infections (CNS, pneumonia) and two for other reasons (acid peptic disease).

Recent reports show a mortality rate of 1.96% to 3% among hospitalized SLE patients; active SLE (severe renal disease), infection, and APAS were the most common causes of death.[26-28] We reported a higher mortality rate of 9% in our cohort and the causes of death were bleeding complications (intracranial and pulmonary) in two and pulmonary infection in two others. Common findings among our patients who died were high disease activity scores, at least one positive serologic test, multiple organ involvement including hematologic disorder, and use of high dose glucocorticoids or pulse therapy. One of these patients was given rituximab.

This study has several limitations. Since the study recruited only the service patients of the hospital, the results cannot be applied to the general population of lupus in the Philippines. It used a modified definition of the LLDAS because the study was retrospective and immunologic tests were rarely monitored in the clinic, thus some information required in the standard LLDAS were not available. It is possible that the modified definition may overestimate the degree of lupus control. The size of our cohort is small and some data that may affect outcomes like personal or family

income, and frequency of follow-up were not collected. To address these, a prospective study with a larger number of patients with longer follow-up is ideal. The collection of information on reasons for readmission and assessments for organ damage that may be subclinical (e.g., cataract) are best collected in a prospective manner and provides further justification for the establishment of a patient registry.

CONCLUSION

In our cohort of 44 newly-diagnosed patients with lupus managed in a tertiary government hospital in Manila, Philippines in 2018-2019, remission rate was very low (2.3%) and mLLDAS was achieved in 34% at 6-months and 68% at 1-year post-diagnosis. Organ damage, commonly renal, occurred in 15.9%. Only a third (38.8%) of the hospitalizations occurred post-diagnosis and the 30-day readmission rate was 14.7% (5/34). Most of the hospitalizations and organ damage occurred during the first six months of follow-up and decreased over time. All mortalities occurred during the first hospitalization for lupus.

There is a need to look into processes and treatment protocols for lupus and to advocate for better education and financial support to improve outcomes among our patients.

Statement of Authorship

Both authors contributed equally (conceptualization of work, acquisition and analysis of data, drafting and revising of manuscript; and final approval of the version to be published) to the paper.

Author Disclosure

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