

# COMMUNITY-ACQUIRED PNEUMONIA IN THAI PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Roongtiva Narata, Suparaporn Wangkaew, Nuntana Kasitanon and Worawit Louthrenoo

Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University Hospital, Chiang Mai, Thailand

**Abstract.** Infection, particularly pneumonia, is a major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE). This study was performed to assess the prevalence, causative organisms, and outcomes of community-acquired pneumonia (CAP) in Thai SLE patients, and determine the predicting factors for death. A retrospective chart review of adult SLE patients, age >16 years, seen at the Division of Rheumatology, Chiang Mai University over an 18 year period was carried out. Cases diagnosed with CAP were selected for this study. Of 542 SLE patients, a total of 56 episodes of CAP occurred in 52 patients. Their mean age  $\pm$  SD and duration of SLE were  $37.98 \pm 11.48$  years and  $34.99 \pm 54.53$  months, respectively. Thirty-three CAP cases (58.9%) occurred within the first year of diagnosis with SLE. The causative organisms identifiable in 40 patients (71.5%) were *Mycobacterium tuberculosis* in 12, *Nocardia* spp in 6, *Aspergillus* spp in 5, *Staphylococcus aureus* in 3, *Pneumocystis carinii*, *Haemophilus influenzae*, *Escherichia coli*, and *Pseudomonas aeruginosa* in 2 each, and *Acinetobacter baumannii*, *Burkholderia pseudomallei*, and *Strongyloides stercoralis* in 1 each. The remaining 3 patients had mixed bacterial infection. The overall mortality rate was 26.8%. Use of high dose prednisolone ( $\geq 15$  mg/day), and ventilator support were significantly associated with death.

## INTRODUCTION

Systemic lupus erythematosus (SLE), which is an autoimmune disease characterized by multiple organ inflammation, primarily affects young adults, and can cause significant morbidity and mortality (Abu-Shakra *et al*, 1995; Ward *et al*, 1995; Cervera *et al*, 1999; Bellomio *et al*, 2000; Kasitanon *et al*, 2006). The use of corticosteroids and immunosuppressive drugs, along with early diagnosis and the general improvement in medical care, have resulted in an improvement in morbidity and mortality in the past few decades. However, infection remains the major cause of morbidity

and mortality in these patients, particularly in developing countries (Leoung *et al*, 1997; Paton, 1997; Kim *et al*, 1999; Bellomio *et al*, 2000; Kasitanon *et al*, 2002; Bosch *et al*, 2006). Factors related to infection in SLE include disease activity, SLE related abnormalities in both humoral and cellular immune responses, and the use of corticosteroids and immunosuppressive therapy (Staples *et al*, 1974; Duffy *et al*, 1991; Petri and Genovese, 1992; Noel *et al*, 2001; Bosch *et al*, 2006; Falagas *et al*, 2006).

Several studies in Thailand, including our previous report, have shown that infection, particularly pneumonia, is the major cause of morbidity and death in these patients (Nanagara *et al*, 1990; Janwityanuchit *et al*, 1993; Kasitanon *et al*, 2002; Wongchinsri *et al*, 2002). Details of the clinical features of pneumonia, its relationship to the clinical activity of SLE and its outcome in Thai patients

---

Correspondence: Dr Worawit Louthrenoo, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.

Tel: +66-53-946449, Fax: +66-53-357959

E-mail: wlouthre@mail.med.cmu.ac.th

with SLE, have never been studied. The aim of this study was to describe the prevalence, causative organisms, clinical features, laboratory findings, and outcomes in community acquired pneumonia (CAP) in Thai patients with SLE, and analyze the predicting factors for death in these patients.

## PATIENTS AND METHODS

The medical records for all adult patients (over 16 years old), who were diagnosed with SLE, treated at the Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University from October 1986 to October 2004, were reviewed. The diagnosis of SLE followed the criteria developed by the American College of Rheumatology (Tan *et al*, 1982; Hochberg, 1997). Only cases with a diagnosis of CAP were included in this study.

The diagnosis of CAP required at least 3 of the following 5 criteria (fever, cough, dyspnea, pleuritic chest pain during inspiration, and auscultation of crepitation sounds) plus radiographic evidence of pulmonary infiltrations and response to appropriate antibiotics. Microbial pathogens were identified by (1) isolation of the organisms from sputum, pleural fluid, bronchoalveolar lavage (BAL) fluid, or blood, and (2) a pathological report from a lung biopsy, necropsy, or autopsy.

SLE disease activity was determined by the Mexican version of the Systemic Lupus Erythematosus Disease Activity Index – MEX-SLEDAI (Guzman *et al*, 1992). The daily dosage and accumulative dose of corticosteroids and immunosuppressive drugs at 15 days prior to the development of CAP were recorded. The cumulative dose was calculated by the mean daily dose multiplied by the number of days. For patients who received intravenous corticosteroids (*eg*, dexamethasone or methylprednisolone) or oral dexamethasone, the dosage was calculated to the equivalent

of that for prednisolone. For those who received intravenous cyclophosphamide, the total monthly infusion dose was divided by 30 to become a daily dose.

The study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University.

## Statistical analysis

The SPSS (version 10) statistical program (SPSS Inc, Chicago, Illinois, USA) was used for statistical analysis. Continuous variables were described as mean  $\pm$  standard deviation (SD), and categorical variables were described as number or percentages. Univariate analysis was used to compare the difference between patients who died and those who survived. A *p*-value of  $<0.05$  was considered clinically significant.

## RESULTS

Of 542 patients reviewed, a total of 56 CAP episodes occurred in 52 patients (4 men and 48 women, with a mean age  $\pm$  SD of  $37.98 \pm 11.48$  years, and mean duration of SLE  $\pm$  SD of  $34.99 \pm 54.53$  months). Thirty-three CAP cases (58.9%) occurred within the first year of diagnosis of SLE, 11 (19.6%) occurred on initial presentation with the diagnosis of SLE and 22 (39.3%) occurred after the diagnosis of SLE was made, with a mean duration of  $4.48 \pm 3.60$  months. The remaining 23 cases (41.1%) occurred with a mean duration after the diagnosis of SLE of  $80.91 \pm 60.23$  months, or  $6.74 \pm 5.01$  years. Forty-two CAP cases (75.0%) occurred in patients who received prednisolone at a mean daily dosage and mean cumulative dosage within 15 days of the CAP episode of  $29.76 \pm 18.61$  mg/day and  $454.64 \pm 275.76$  mg, respectively. Twelve patients (28.6%) also received an immunosuppressive drug (cyclophosphamide in all patients) with a mean daily dose and mean cumulative dosage within 15 days of being diagnosed with CAP of  $66.66 \pm 24.62$  mg/day

and  $945.83 \pm 345.39$  mg, respectively. The mean MEX-SLEDAI score at the time of CAP diagnosis was  $5.69 \pm 5.28$ .

In 56 CAP cases, the causative organisms were identified by sputum, BAL fluid cultures or blood cultures in 40 cases (71.4%). Bacterial pneumonia was the most common form of CAP, seen in 14 cases (25.0%). Three patients had mixed bacterial infection. *Mycobacterium tuberculosis* was the second most common cause of CAP, seen in 12 cases. In 10, the organism was identified in sputum, or BAL fluid smears or cultures. The remaining 2 patients, in whom the organism was not identified, had chest radiographs that were consistent with pulmonary tuberculosis, and the infiltration was resolved completely after anti-tuberculous drug therapy. Five of these 12 patients also had evidence of tuberculous infection in other organs, such as the skin, kidney, bone or lymph node. The remaining causative organisms responsible for CAP were *Nocardia* spp in 6 cases, *Aspergillus* spp in 5 (of which 3 organisms were identified by a pathology report of the lymph node or a lung

biopsy), *Pneumocystis carinii* in 2 (the organism was not identifiable in 1 patient, but the clinical and chest radiograph improved after anti-*Pneumocystis carinii* therapy), and *Strongyloides stercoralis* in 1 case (Table 1).

Fever was the most common presenting symptom in 47 cases (83.9%). It ranged from 38.0°C to 40.4°C with a mean temperature of  $38.38 \pm 1.00$ °C. Cough, dyspnea and pleuritic chest pain were among the common chest symptoms, and were seen in 33 (58.9%), 16 (28.6%) and 5 (8.9%) cases, respectively. Five patients (8.9%) did not have any chest symptoms, but had infiltrations on chest radiographs. Details of the symptoms and their mean duration  $\pm$  SD before the diagnosis of CAP were made according to the group of microbial organisms, are shown in Table 2.

Laboratory and chest radiographic findings are shown in Table 3. The causative organisms were identified by sputum smears or cultures in approximately one third of the cases, and by BAL fluid cultures in an additional 7.1%. Only 19.6% of the cases had positive blood cultures. Abnormal chest radio-

Table 1

Forty identified organisms among 56 community acquired pneumonia (CAP) patients with SLE.

Organism	No.	%
<i>Staphylococcus aureus</i>	3	7.5
<i>Haemophilus influenzae</i>	2	5
<i>Escherichia coli</i>	2	5
<i>Pseudomonas aeruginosa</i>	2	5
<i>Acinetobacter baumannii</i>	1	2.5
<i>Burkholderia pseudomallei</i>	1	2.5
<i>Streptococcus pneumoniae</i> + <i>H. influenzae</i> + <i>Mycoplasma catarrhalis</i>	1	2.5
<i>S. aureus</i> + <i>P. aeruginosa</i>	1	2.5
<i>P. aeruginosa</i> + <i>S. viridans</i>	1	2.5
<i>Mycobacterium tuberculosis</i>	12	30
<i>Nocardia</i> spp	6	15
<i>Aspergillus</i> spp	5	12.5
<i>Pneumocystis carinii</i>	2	5
<i>Strongyloides stercoralis</i>	1	2.5
Total	40	100

Table 2  
Chest symptoms and mean duration of symptoms before the diagnosis of CAP was made  
(by groups of microorganisms).

Organisms	Fever No. (%)	Cough No. (%)	Dyspnea No. (%)	Pluritis No. (%)	Mean duration of symptoms in days $\pm$ SD (Median)
Unknown (n=16)	14 (87.5)	11 (68.8)	5 (31.2)	1 (6.2)	7.13 $\pm$ 7.74 (4.50)
<i>M. tuberculosis</i> (n=12)	10 (83.3)	5 (41.7)	5 (41.7)	2 (16.7)	22.64 $\pm$ 25.52 (14.00)
<i>Nocardia</i> spp (n=6)	4 (66.7)	2 (33.3)	1 (16.7)	1 (16.7)	8.40 $\pm$ 12.38 (4.00)
<i>Aspergillus</i> spp (n=5)	5 (100.0)	4 (80.0)	1 (20.0)	1 (20.0)	62.80 $\pm$ 67.60 (30.00)
<i>Strongyloides stercoralis</i> (n=1)	1 (100.0)	1 (100.0)	0 (0.0)	0 (0.0)	10.00 $\pm$ 0.00 (10.00)
<i>Pneumocystis carinii</i> (n=2)	2 (100.0)	1 (50.0)	0 (0.0)	0 (0.0)	1.00 $\pm$ 0.00 (1.00)
Bacteria (n=14)	11 (78.6)	9 (64.3)	5 (35.7)	1 (7.1)	13.93 $\pm$ 17.49 (6.00)

Table 3  
Laboratory and chest radiographic findings.

Laboratory results	N = 56
Complete blood count (CBC) (mean $\pm$ SD)	
Hemoglobin level (g/dl)	9.61 $\pm$ 2.01
White Blood Cell count ( $\times 10^3/\text{mm}^3$ )	8.38 $\pm$ 5.65
PMN (%)	80.40 $\pm$ 11.56
Blood chemistry (mean $\pm$ SD)	
Creatinine (mg/dl)	1.43 $\pm$ 0.95
Positive stain sputum (%)	18 (32.1)
Positive sputum culture (%)	19 (33.9)
Positive BAL culture (%)	4 (7.1)
Positive hemoculture (%)	11 (19.6)
Positive from pathological report (%)	6 (10.7)
Chest X ray (%)	
Localized patchy infiltration	20 (35.7)
Bilateral alveolar or multilobar infiltration	14 (25.0)
Pleural effusion	9 (16.1)
Interstitial/reticulonodular infiltration	7 (12.5)
Cavitary lesion	5 (9.9)
Atelectasis	1 (1.8)

graphs were found in all cases. Localized patchy infiltration was the most common chest radiographic finding, found in 35.7% of cases. Most of these radiographic findings were caused by bacterial infection. Bilateral reticulonodular infiltration was the second most common radiographic finding, found in 25.0% of patients. This radiographic finding

was caused by *M. tuberculosis* in 10.7%. Three of 5 patients who had cavitary lesions were caused by *Nocardia* spp (5.3%).

Complications of CAPs were seen in 26 patients (46.4%). These were respiratory failure requiring ventilatory support in 15 cases (26.8%), acute respiratory distress syndrome in 4 (7.1%), hospital acquired pneumonia in 3

Table 4  
Univariate analysis of potential risk factors for death in CAP in patients with SLE.

Factors	Death (n=15)	Survive (n=41)	p
Sex (M/F) (no.)	0/15	4/37	0.260
Age (years)	37.20 ± 11.42	38.27 ± 11.63	0.761
Mean disease duration of SLE (months)	20.76 ± 38.68	40.20 ± 58.83	0.241
Mean MEX-SLEDAI score at onset of pneumonia	8.13 ± 6.32	4.74 ± 4.56	0.033
Mean duration of CAP before treatment (days)	17.87 ± 16.70	16.87 ± 32.37	0.911
Number taking prednisolone (%)	12 (80.0)	30 (73.2)	0.736
Mean daily dosage of prednisolone (mg/day)	41.25 ± 15.97	25.17 ± 17.79	0.010
Cumulative dose of prednisolone 15 days prior to episode of CAP (mg/day)	596.25 ± 232.57	37.00 ± 268.08	0.014
Mean duration of receiving prednisolone therapy (days)	83.25 ± 105.51	360.30 ± 984.96	0.340
Number taking immunosuppressive drugs (%)	6 (40.0)	6 (14.6)	0.064
Mean dosage of cyclophosphamide (mg/day)	26.61 ± 37.16	9.76 ± 25.54	0.059
Cumulative dose of cyclophosphamide 15 days prior to episode of CAP (mg/day)	1,000.00 ± 387.29	891.67 ± 324.68	0.611
Mean duration of receiving cyclophosphamide therapy (days)	102.83 ± 98.57	41.00 ± 40.52	0.186
Hb <12.00 mg/dl (%)	13 (86.7)	35 (85.4)	1.000
Leukopenia (<4,000/mm <sup>3</sup> ) (%)	3 (20.0)	9 (21.9)	0.062
Leukocytosis (>10,000/mm <sup>3</sup> ) (%)	3 (20.0)	11 (26.8)	0.736
Renal insufficiency (Cr >1.40 mg/dl) (%)	7 (46.7)	21 (51.2)	1.000
Hypoalbuminemia (<3.00 gm/dl)	10 (66.7)	23 (56.1)	0.685
Respiratory failure with ventilator support (%)	12 (80.0)	3 (7.3)	< 0.001

(5.3%), septic shock in 2 (3.6%) and disseminated intravascular coagulation in 2 (3.6%). Fifteen patients died, giving a mortality rate of 26.8%. Death occurred in 3 of 14 patients with bacterial CAP (21.4%), 1 of 12 with *M. tuberculosis* (8.3%), 1 of 6 with *Nocardia* spp (16.7%), 3 of 5 with *Aspergillus* spp (60.0%), and 1 of 1 patient with *S. stercoralis* pneumonia (100.0%). Six deaths (37.5%) occurred in 16 CAP cases in whom the organism was not identifiable.

The risk factors for death in SLE patients with CAP are shown in Table 4. None of the clinical or laboratory variables (age, sex, disease duration, duration of corticosteroid or immunosuppressive treatment, presence of anemia, white blood cell count, renal insufficiency, or hypoalbuminemia) predicted an outcome of death. On univariate analysis, a high

lupus activity (MEX-SLEDAI score) at the onset of pneumonia, a high mean daily dose of prednisolone, a mean cumulative dose of prednisolone 15 days prior to the development of CAP, and respiratory failure with ventilator support were the risk factors for death ( $p < 0.005$ ). However, on multivariate analysis, respiratory failure with ventilator support and a mean daily dose of prednisolone  $\geq 15$  mg/day at the onset of CAP, were the only 2 risk factors for death ( $p = 0.024$  and  $p = 0.045$ , respectively).

## DISCUSSION

In this study, we found a CAP prevalence of 10.3%. Approximately 60% occurred within the first year of SLE diagnosis; one fifth occurred simultaneously with the diagnosis of SLE and the remainder occurred after SLE was

diagnosed with a mean duration  $\pm$  SD of  $4.48 \pm 3.60$  months. CAP occurred while patients were taking corticosteroids or immunosuppressive drugs in 75.0% and 28.6%, respectively. The causative organism was identified in 71.4% of cases; bacteria and *M. tuberculosis* were the two most common organisms (25.0% and 21.4%, respectively). Opportunistic pathogens (eg, fungus and *Nocardia* spp) were not uncommon. Fever, dyspnea, cough and abnormal pulmonary infiltration were the most common presenting symptoms. These were similar to pneumonia in the general population. However, 8.9% of CAP cases in SLE patients did not have any chest symptoms, but had abnormal infiltration on chest radiographs. Fifteen patients died, giving a mortality rate of 26.8%. Respiratory failure with mechanical ventilator support, and daily prednisolone at the onset of CAP were the only 2 factors associated with death.

Previous studies of pneumonia in SLE patients in Thailand are limited. Janwityanuchit *et al* (1993), in their retrospective study of 265 SLE patients at Ramathibodi Hospital, found 49 cases of pneumonia (18.5%). Of the 33 identifiable organisms, *M. tuberculosis* was found in 16 cases, *Streptococcus* spp in 4, *Klebsiella* spp in 4, *Nocardia* spp in 3, anaerobic bacteria and *Aspergillus* spp in 2, and *Cryptococcus* spp and *B. pseudomallei* in 1. Wongchinsri *et al* (2002) found that infections caused the hospitalization in 191 of 488 SLE patients at King Chulalongkorn Memorial Hospital; 47 cases (24.6%) were due to pulmonary infection. Of the 35 in whom the organism was identified, bacterial infection was found in 14 cases (40.0%), *M. tuberculosis* in 9 (25.7%), *Nocardia* spp in 7 (20.0%), *P. carinii* in 4 (11.4%) and *Aspergillus* spp in 1 case (2.8%). In a study of 230 CAP cases at Srinagarind Hospital by Reechaipichitkul *et al* (2002), 8 of 120 CAP cases, in which the organism was identified occurred in patients with connective tissue diseases; the organisms

were *S. aureus* in 3 cases, *S. pneumoniae* in 3 and *B. pseudomallei* in 2. They also found that patients with connective tissue disease or those using corticosteroids were at risk for *K. pneumoniae*, *B. pseudomallei*, *H. influenzae*, and *S. aureus* pneumonia.

Details of pneumonia in SLE patients from western countries are also limited. Duffy *et al* (1991) found that infection was the cause of hospitalization in 53 of their 81 SLE patients; 10 (18.9%) had pneumonia. Gram-negative organisms, such as *P. aeruginosa*, *H. influenzae*, *S. marcescens*, *K. pneumoniae* and *Legionella* spp were the most common responsible organisms. There was only 1 case of *M. tuberculosis* pulmonary infection. No cases of *Nocardia* spp or fungal lung infections were identified. They also found that infection was associated with active lupus (high disease activity index). A recent controlled study showed that poor oral hygiene and dental caries were significant risk factors for pneumonia in SLE patients (Pascual-Ramos *et al*, 2006).

Our results are in line with previous reports in Thailand, in that pneumonia was the most common infection in SLE patients. Bacteria and *M. tuberculosis* were the two most common causative organisms. *Nocardia* spp and fungal infection were not uncommon (Janwityanuchit *et al*, 1993; Wongchinsri *et al*, 2002). These results differed from western countries in that bacteria were the most common offending organisms, whereas *M. tuberculosis*, *Nocardia* spp and fungal pneumonia were uncommon.

*M. tuberculosis* was the second most common cause of CAP in this study. It should be noted that 41.7% of our cases also had extra-pulmonary infection. Our results are similar to those of Yun *et al* (2002), who recently reviewed *M. tuberculosis* infection in 283 Korean SLE patients. Twelve of their patients had pulmonary infection. Fifty percent of their cases also had extra-pulmonary involvement. In their study, patients who took a higher dose

of prednisolone or immunosuppressive drugs were more prone to develop *M. tuberculosis* infection than those who took a lower dose.

The presence of *Nocardia* spp, *Aspergillus* spp, and *P. carinii* pulmonary infection in our study was not surprising, as the majority of our patients received corticosteroids or immunosuppressive therapy for their disease. Nocardiosis in SLE patients has been well described and reviewed (Mok *et al*, 1997). The incidence of *Nocardia* spp infection in SLE ranged between 0.6 and 2.8% (Mok *et al*, 1997; Leong *et al*, 2000). Lung involvement was seen in approximately 80.0% of these cases. The mortality rate was 35.0%. The diagnosis of pulmonary nocardiosis in SLE is difficult and an aggressive diagnostic approach is often required as there are no pathognomonic chest radiographic findings. Pulmonary infiltrations or nodules with cavitations are common findings. We found that 3 of 5 patients who had cavitary lesions on chest radiographs were due to *Nocardia* spp. *Nocardia* infection in SLE has been reported as more common in those being treated with a higher dosage of prednisolone (Mok *et al*, 1997). However, we found no significant difference in the mean daily dose of prednisolone between patients with pneumonia caused by *Nocardia* spp and those caused by other organisms ( $46.67 \pm 9.83$  mg/day vs  $31.92 \pm 18.67$  mg/day;  $p=0.14$ ).

Aspergillosis in patients with SLE has been reported infrequently. A recent reviewed showed that it usually occurred in patients who had high disease activity, received high dose corticosteroids or immunosuppressive drugs, had granulocytopenia or had bacterial infection (Gonzalez-Crespo and Gomez-Reino, 1995; Katz *et al*, 1996). The mortality rate was extremely high (95.6%). The diagnosis was usually made postmortem. In this study, none of our patients received immunosuppressive drugs, and only one patient had leukopenia. The mortality rate was 60.0%.

Pneumonia caused by *P. carinii* also has been well recognized in patients with SLE and connective tissue diseases (Godeau *et al*, 1994; Kadoya *et al*, 1996; Li *et al*, 2006). The majority of the patients developed *P. carinii* pneumonia shortly after the diagnosis of connective tissue diseases (3-8 months), and most were receiving corticosteroids or immunosuppressive drugs. Most patients were leukopenic. Fever, dry cough, and interstitial pulmonary infiltration were the most common presentations. The duration of symptoms was much shorter than those that occurred in patients with human immunodeficiency virus infection. The diagnosis usually required examination of the BAL fluid or a lung biopsy.

On univariate analysis, a high disease activity score, high mean daily dose of corticosteroids, cumulative dose of corticosteroids, use of immunosuppressive drugs (or cyclophosphamide), and respiratory failure with ventilator support were found to be risk factors for death in SLE patients with CAP. On the multivariate analysis, only mean daily dosage of corticosteroids ( $\geq 15$  mg/day) and respiratory failure with ventilator support were independent factors that predicted death. Our findings are consistent with those of Hellmann *et al* (1987), who found that corticosteroids and immunosuppressive drugs use within 3 months prior to admission were associated with death.

In conclusion, in addition to bacterial pneumonia, *M. tuberculosis* and other opportunistic pathogens were commonly found as causes of CAP in Thai SLE patients. CAP usually occurred within the first year of SLE diagnosis, when the disease was active and the patients required high dose corticosteroids or immunosuppressive drugs. The mortality rate for SLE patients who had CAP was high. Rapid, and sometimes, aggressive investigations to identify the organisms responsible for pulmonary infections or pulmonary infiltrations, with a prompt start of appropriate antibiotics,

should be done in SLE patients who receive high dose corticosteroids and immunosuppressive drugs, in order to decrease morbidity and mortality.

## REFERENCES

- Abu-Shakra M, Urowitz MB, Gladman DD, Gouch J. Mortality studies in systemic lupus erythematosus. Results from a single center. I. Causes of death. *J Rheumatol* 1995; 22: 1259-64.
- Bellomio V, Spindler A, Lucero E, *et al.* Systemic lupus erythematosus: mortality and survival in Argentina. A multicenter study. *Lupus* 2000; 9: 377-81.
- Bosch X, Guilabert A, Pallares L, *et al.* Infections in systemic lupus erythematosus: a prospective and controlled study of 110 patients. *Lupus* 2006; 15: 584-9.
- Cervera R, Khamashta MA, Font J, *et al.* Morbidity and mortality in systemic lupus erythematosus during a 5-year period. A multicenter prospective study of 1,000 patients. European Working Party on Systemic Lupus Erythematosus. *Medicine (Baltimore)* 1999; 78: 167-75.
- Duffy KN, Duffy CM, Gladman DD. Infection and disease activity in systemic lupus erythematosus: a review of hospitalized patients. *J Rheumatol* 1991; 18: 1180-4.
- Falagas ME, Manta KG, Betsi GI, Pappas G. Infection-related morbidity and mortality in patients with connective tissue diseases: a systematic review. *Clin Rheumatol* 2006; Dec 21; [Epub ahead of print].
- Godeau B, Coutant-Perronne V, Le Thi Huong D, *et al.* *Pneumocystis carinii* pneumonia in the course of connective tissue disease: report of 34 cases. *J Rheumatol* 1994; 21: 246-51.
- Gonzalez-Crespo MR, Gomez-Reino JJ. Invasive aspergillosis in systemic lupus erythematosus. *Semin Arthritis Rheum* 1995; 24: 304-14.
- Guzman J, Cardiel MH, Arce-Salinas A, Sanchez-Guerrero J, Alarcon-Segovia D. Measurement of disease activity in systemic lupus erythematosus. Prospective validation of 3 clinical indices. *J Rheumatol* 1992; 19: 1551-8.
- Hellmann DB, Petri M, Whiting-O'Keefe Q. Fatal infections in systemic lupus erythematosus: the role of opportunistic organisms. *Medicine (Baltimore)* 1987; 66: 341-8.
- Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997; 40: 1725.
- Janwityanuchit S, Totemchokchayakarn K, Krachangwongchai K, Vatanasuk M. Infection in systemic lupus erythematosus. *J Med Assoc Thai* 1993; 76: 542-8.
- Kadoya A, Okada J, Iikuni Y, Kondo H. Risk factors for *Pneumocystis carinii* pneumonia in patients with polymyositis/dermatomyositis or systemic lupus erythematosus. *J Rheumatol* 1996; 23: 1186-8.
- Kasitanon N, Louthrenoo W, Sukitawut W, Vichainun R. Causes of death and prognostic factors in Thai patients with systemic lupus erythematosus. *Asian Pac J Allergy Immunol* 2002; 20: 85-91.
- Kasitanon N, Magder LS, Petri M. Predictors of survival in systemic lupus erythematosus. *Medicine (Baltimore)* 2006; 85: 147-56.
- Katz A, Ehrenfeld M, Livneh A, *et al.* Aspergillosis in systemic lupus erythematosus. *Semin Arthritis Rheum* 1996; 26: 635-40.
- Kim WU, Min JK, Lee SH, Park SH, Cho CS, Kim HY. Causes of death in Korean patients with systemic lupus erythematosus: a single center retrospective study. *Clin Exp Rheumatol* 1999; 17: 539-45.
- Leong KP, Tee NW, Yap WM, Chee TS, Koh ET. Nocardiosis in patients with systemic lupus erythematosus. The Singapore Lupus Study Group. *J Rheumatol* 2000; 27: 1306-12.
- Leoung KH, Koh ET, Feng PH, Boey ML. The clinical outcome of 100 SLE patients after 5-years of follow up. *APLAR J Rheumatol* 1997; 1: 23-6.
- Li J, Huang XM, Fang WG, Zeng XJ. *Pneumocystis carinii* pneumonia in patients with connective tissue disease. *J Clin Rheumatol* 2006; 12: 114-7.
- Mok CC, Yuen KY, Lau CS. Nocardiosis in systemic lupus erythematosus. *Semin Arthritis Rheum*



- 1997; 26: 675-83.
- Nanagara R, Nantiruj K, Laopaiboon M. Clinical study of the outcome in systemic lupus erythematosus: causes of death and prognostic factors. *Intern Med (Thailand)* 1990; 6: 1-5.
- Noel V, Lortholary O, Casassus P, *et al.* Risk factors and prognostic influence of infection in a single cohort of 87 adults with systemic lupus erythematosus. *Ann Rheum Dis* 2001; 60: 1141-4.
- Pascual-Ramos V, Hernandez-Hernandez C, Soto-Rojas AE, Celis-Aguilar E, Sanchez-Guerrero J. Association between dental caries and pneumonia in patients with systemic lupus erythematosus. *J Rheumatol* 2006; 33: 1996-2002.
- Paton NI. Infections in systemic lupus erythematosus patients. *Ann Acad Med Singapore* 1997; 26: 694-700.
- Petri M, Genovese M. Incidence of and risk factors for hospitalizations in systemic lupus erythematosus: a prospective study of the Hopkins Lupus Cohort. *J Rheumatol* 1992; 19: 1559-65.
- Reechaipichitkul W, Lulitanond V, Tantiwong P, Saelee R, Pisprasert V. Etiologies and treatment outcomes in patients hospitalized with community-acquired pneumonia (CAP) at Srinagarind Hospital, Khon Kaen, Thailand. *Southeast Asian J Trop Med Public Health* 2005; 36: 156-61.
- Staples PJ, Gerding DN, Decker JL, Gordon RS, Jr. Incidence of infection in systemic lupus erythematosus. *Arthritis Rheum* 1974; 17: 1-10.
- Tan EM, Cohen AS, Fries JF, *et al.* The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; 25: 1271-7.
- Ward MM, Pyun E, Studenski S. Causes of death in systemic lupus erythematosus. Long-term followup of an inception cohort. *Arthritis Rheum* 1995; 38: 1492-9.
- Wongchinsri J, Tantiwichien T, Osiri M, Akkasilpa S, Deesomchok U. Infection in Thai patients with systemic lupus erythematosus: a review of hospitalized patients. *J Med Assoc Thai* 2002; 85 (suppl 1): S34-9.
- Yun JE, Lee SW, Kim TH, *et al.* The incidence and clinical characteristics of *Mycobacterium tuberculosis* infection among systemic lupus erythematosus and rheumatoid arthritis patients in Korea. *Clin Exp Rheumatol* 2002; 20: 127-32.