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Spectrum of Infection among Admitted Systemic Lupus Erythematosus Patients

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Abstract

Background: Patients of Systemic Lupus Erythematosus (SLE) often require hospitalisation due to infections, which remains a major cause of mortality and morbidity in these patients. This study was intended to study the spectrum of infection and clinical profile of SLE patients getting admitted at a tertiary centre in north India.

Methods: This was a cross-sectional observational study done over a period of one year on SLE patients' getting admitted under the department of medicine with suspected infection. The demographic, presenting complaints, duration of SLE, treatment history, clinical parameters, laboratory investigations, SLE-related organ involvement, systemic lupus erythematosus disease activity score (SLEDAI) at admission, type of infection, duration of hospital stay, treatment received, and outcome were recorded.

Results: A total of 27 patients were included in the study and the mean age of the patients was 29.7 ± 10.7 years. The most common symptom at the time of admission in the hospital was fever (74%), followed by cough (55%), dyspnoea (55%), oral ulcers (51%), arthralgia (37%), photosensitivity (33%), oliguria (15%), and psychosis (11%). The common risk factors for infection seen in this study were steroid intake in the last 3 months (51.8%), previous antibiotic intake (18.5%), other immunosuppressant therapy (18.5%), recent hospital stay (7.4%) and past history of tuberculosis (7.4%). Acute phase reactants were significantly elevated and mean SLEDAI score was 11.1 ± 6.8.

The most common infection was bacterial pneumonia (44.4%), followed by tuberculosis (33.3%), fungal pneumonia (7.4%), MRSA bacteraemia (7.4%), acute gastroenteritis (7.4%), urinary tract infection (7.4%), skin infection (3.7%), HIV (3.7%) and infective endocarditis (3.7%). E.coli, Methicillin resistant Staphylococcus aureus (MRSA), A.baumannii and Candida were isolated from various specimens. There were four deaths due to infection.

Conclusion: Bacterial pneumonia and tuberculosis are the leading cause of infection among hospitalised SLE patients.

Key words: Fungal infection, Staphylococcus aureus, tuberculosis.

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterised by multiple organ involvement requiring long-term immunosuppressant therapy. SLE patients have two- to five-fold increased mortality as compared to the general population[1-2]. The mortality in SLE has a bi-modal pattern with earlier deaths due to high disease activity and the later deaths related to various complications of SLE like cardiovascular disease and malignancy[3-4]. Infections in SLE can occur during any stage of the disease and often correlate with high disease activity. However, Indian data suggests both high disease activity and infection as the leading causes of mortality in these patients[5]. Impairment of both innate and adaptive immunity in SLE along with use of immunosuppressant therapy predisposes them to various infections[6]. This study was intended to study the spectrum of infection and clinical profile of SLE patients getting admitted at a tertiary centre in north India.

Subjects and Methods

This was a cross-sectional observational study done in the Department of Medicine at the All India Institute of Medical Sciences, New Delhi. The study was approved by the ethical committee of the institute. All patients satisfying either 1997 American College of Rheumatology Modified Classification Criteria or the 2012 Systemic Lupus International Collaborating Clinics Classification Criteria for the diagnosis of SLE getting admitted in the hospital between June 2018 and June 2019 with a provisional diagnosis of infection were included in the study. Patients having overlap syndrome and only flare without any

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infection were excluded from the study. Infection was defined by presence of three of the following clinical criteria: fever, increase in acute phase reactants (CRP, ESR) or procalcitonin, leucocytosis, presence of focal abnormalities (like lung infiltrates, leucocyturia, cellulitis, etc.,) and good response to antibiotics.

The demographic, presenting complaints, duration of SLE, treatment history, clinical parameters, laboratory investigations, SLE-related organ involvement, systemic lupus erythematosus disease activity score (SLEDAI) at admission, type of infection, duration of hospital stay, treatment received, and outcome, were recorded on a pre-designed proforma.

Statistical analysis

The statistical analysis was performed using Stata 13 software. Continuous variables were expressed as mean and standard deviation (SD) or median and range (if any outliers). Qualitative variables were summarised as frequency and percentage.

Results

There were a total of 27 patients in the study; female to male ratio was 26:1. The mean age of the patient was 29.7 ± 10.7 years and mean duration of hospital stay was 12.2 ± 7.8 days. The median duration of SLE was 12 months (range: 0 - 156 months) and 6 patients were newly detected cases of SLE (Table I). The most common symptom at the time of admission in the hospital was fever (74%), followed by cough (55%), dyspnoea (55%), oral ulcers (51%), arthralgia (37%), photosensitivity (33%), oliguria (15%), and psychosis (11%). The most common risk factor associated with infection was steroid intake in the last 3 months (51.8%), followed by previous antibiotic intake (18.5%), other immunosuppressant therapy (18.5%), recent hospital stay (7.4%) and past history of tuberculosis (7.4%) (Table II).

Table I: Demographic and Clinical features of admitted SLE patients.

Variables	Mean ± standard deviation
Age	29.7 ± 10.7 years
Duration of SLE	Range: 0 to 156 months; median: 12 months
Duration of hospital stay	12.2 ± 7.8 days
SLEDAI score	11.1 ± 6.8

The mean haemoglobin level was 7.7 ± 1.9 gm/dl, total leukocyte count (7,441± 7,046), platelet count (1,43,148 ± 1,14,136), urea (77.6 ± 55.8 mg/dl), creatinine (1.3 ± 0.9), ESR (65.7 ± 21.3 mm/hr), CRP (79.9 ± 67.3 mg/l), ferritin (1,840 ± 2,022 ng/ml), n = 15] (Table III). The mean SLEDAI score was 11.1 ± 6.8, suggestive of mild-to-moderate flare. Among the organs affected due to SLE per se, the most commonly affected organ was renal (70.3%), followed by haematological (59.2%), cardiovascular (25.9%) and neurological (22.2%).

Type II: Various risk factors associated with infection in SLE patients.

Risk factors in last 3 months	Number of patients (%) (n = 27)
Steroid intake	14 (51.8%)
Hospitalisation	2 (7.4%)
Antibiotic intake	5 (18.5%)
Cyclophosphamide	1 (3.7%)
MMF	2 (7.4%)

Table III: Laboratory parameter of SLE patients with infection,

Laboratory parameters	Mean ± standard deviation
Haemoglobin (g/dl)	7.7 ± 1.9
Total leucocyte count (cells/cu mm)	7,441 ± 7,046
Platelet count (cells/cu mm)	1,43,148 ± 1,14,136
Urea (mg/dl)	77.6 ± 55.8
Serum creatinine (mg/dl)	1.3 ± 0.9
ESR (mm/hr)	65.7 ± 21.3
CRP (mg/l)	79.9 ± 67.3

The most common infection was bacterial pneumonia (44.4%), followed by tuberculosis (33.3%), fungal pneumonia (7.4%), MRSA bacteraemia (7.4%), acute gastroenteritis (7.4%), urinary tract infection (7.4%), skin infection (3.7%), HIV (3.7%), and infective endocarditis (3.7%) (Table IV). Among tuberculosis, most common type was extra-pulmonary tuberculosis in 4 patients (14.8%), pulmonary tuberculosis in 3 patients (11.1%), and disseminated tuberculosis in 2 patients (7.4%). Urine culture grew *E.coli* in two patients; two positive blood cultures showed MRSA, and one blood culture was positive for Candida. Sputum culture was sterile in all patients; and broncho-alveolar lavage fluid in one patient grew *Acinetobacter baumannii*. Among various antibiotics administered, the most commonly used was cefoperazone-sulbactam (22.2%), followed by teicoplanin (14.8%), ceftriaxone (14.8%) and azithromycin (14.8%). The outcome was favourable in 23 patients (85%) and there were four mortalities (15%).

Table IV: Spectrum of infection among admitted SLE patients.

Infection type	Number of patients (%) (n = 27)
Bacterial pneumonia	12 (44.4%)
Tuberculosis (All)	9 (33.3%)
Pulmonary tuberculosis	3 (11.1%)
Extra-pulmonary tuberculosis	4 (14.8%)
Disseminated tuberculosis	2 (7.4%)
Fungal pneumonia	2 (7.4%)
MRSA bacteraemia	2 (7.4%)
Acute gastroenteritis	2 (7.4%)
UTI	2 (7.4%)
Skin infection	1 (3.7%)
Infective endocarditis	1 (3.7%)
HIV	1 (3.7%)

Discussion

Infections are the leading cause of mortality and morbidity in patients with SLE. The most common infection in SLE is bacterial, followed by viral and fungal due to impaired immune system. In our study too, we found the most common infection to be bacterial pneumonia, followed by tuberculosis and MRSA bacteraemia. The risk factors associated with infection were steroid use, antibiotic use and past history of tuberculosis.

Among bacterial infections, lower respiratory tract infections (LRTI) are the most common among admitted SLE patients[7]. The common pathogen causing LRTI in SLE patients is *Streptococcus pneumoniae*, followed by *Staphylocoocus aureus*. The risk of *S. pneumoniae* is increased in SLE patients due to defective opsonisation and failure in complement-mediated activation of immune system[8]. Patients on long-term steroid and immunosuppressant therapy are at risk for bacteraemia, which are commonly caused by *S.aureus*, *E. coli,* and *Salmonella*[9-10]. Urinary and skin infections are frequently seen in outpatients. *Gram-negative* pathogens like *E. coli, Kleibsella,* and *Pseudomonas* are commonly involved in urinary tract infections[11]. In our study too, bacterial pneumonia was the most common bacterial infection; however, we could not isolate any organism from sputum samples. MRSA bacteraemia was observed in the present study; and among urinary tract infections, *E. coli* was the most common isolate.

SLE patients are also predisposed to *M.tuberculosis* infections due to dysfunctional immune system and long-term immunosuppressive therapy. The prevalence of *M. tuberculosis* in SLE patients ranges from 5% to 30%[12]. Extrapulmonary tuberculosis is more frequent than pulmonary tuberculosis, and a few patients might acquire multidrug resistant tuberculosis infection too[13-14]. We found tuberculosis to be the second most common infection and we also observed more extra-pulmonary and disseminated cases.

The common viral infections observed in SLE patients are *Herpes zoster*, *cytomegalovirus*, *parvovirus*, *hepatitis B* and *C* and *human papillomavirus*. Opportunistic fungal infections commonly seen in SLE patients are Candida, invasive *aspergillosis*, *Pneumocystis jirovecii* and *Cryptococcus neoformans*[15]. The most common risk factor for opportunistic infections is high disease activity. We had two cases of *aspergillu*s pneumonia and one patient had infective endocarditis due to *Candida*. Disease activity was high in all three patients.

Immune dysfunction is a common predisposing factor in SLE patients. T lymphocytes are reduced in number and T-helper cell activity is impaired in SLE patients with flare[16]. Neutropenia, impaired phagocytic activity and complement dysfunction are other immune defects in these patients[17]. The other risk factors associated with infection are high disease activity, low C3 levels, high anti-dsDNA levels, prednisone dose (> 7.5 mg/day), renal activity, intravenous cyclophosphamide[18-19]. The measures that could be taken to prevent infection rate in SLE patients are yearly influenza vaccination, pneumococcal vaccination, low-dose methylprednisolone pulse, low-dose cyclophosphamide regimen, and hydroxychloroquine therapy in all SLE patients.

Conclusion

Bacterial pneumonia and tuberculosis are the leading cause of infection among SLE patients requiring hospitalisation.

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