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A STUDY OF CLINICAL PROFILE OF INFECTIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS REQUIRING HOSPITALIZATION

Internal Medicine

Dr. Abhishek Dilip Deshmukh* MBBS, MD (Gen. Medicine) Senior resident (RCSM Govt. Medical Collage and CPR hospital Kolhapur. *Corresponding Author

Dr. Sanjay A. Mundhe MBBS, MD (Gen. Medicine), Asso. Professor. Dept of General Medicine,BJ Medical College and Sassoon Hospital, Pune.

Dr. Rohidas T. Borse MBBS, MD (Gen. Medicine) Professor & Head. Dept of General medicine, BJ Medical College and Sassoon Hospital, Pune.

ABSTRACT

Background: Infection is a major source of morbidity and mortality in patients with systemic lupus erythematosus (SLE). Hence the present study focuses on the occurrences of serious infections in SLE patients requiring hospitalization with aim to characterize the infections in terms of organ systems affected, responsible microorganisms, clinical profile, and relation of immunosuppressive drugs. **Method:** This observational study was conducted in total 60 SLE patients who fulfilling SLICC criteria 2012 getting admitted to medicine, dermatology ward or ICU during a period of 18 months. The outcome of cases noted as either death, recovered completely or recovered with sequel. **Results:** Infections in SLE patients were common in 20-30 years age group (38.33%) with female predominance (83.3%). Skin involvement was most common (53.3%). Based on culture positivity urinary tract was most common site of infection (41.66%). All patients who were on cyclosporine/rituximab/MPS had infections (100%). Culture positivity rate was more in patients receiving higher dose of prednisolone (>10mg/day) (66%). Bacteria was the commonest cause of infection (46.6%), and gram-negative bacteria were more common (78.5%). Escherichia coli (35.9%) followed by Klebsiella pneumonae (17.8%) were the commonest bacteria isolated. High SLEDAI score (>11) was found in 62% patients. Significant association was found between SLEDAI score and severity /poor outcome, (p=0.029). Out of 60 patients, 50(84%) recovered completely, 5(8%) recovered with sequelae and death occur in 5(8%) cases. **Conclusion:** Patients of SLE are at increased risk for various infections. SLE is a multisystem disorder affecting predominantly young females. Management of SLE needs vigilance for infection and judicious use of immunosuppressive drugs.

KEYWORDS

Infection; Systemic lupus erythematosus; Immunosuppressive drugs; SLEDAI score

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease affecting many organ systems. There are numerous phenotypes of the disease, with clinical symptoms ranging from modest muco-cutaneous manifestations to multi organ and severe central nervous system involvement in individuals [1]. Several immune-pathogenic mechanisms contribute to the onset of SLE.

Hargraves characterized the lupus erythematosus (LE cell) in 1948. Since then, several pathogenic autoantibodies have been found [2]. The diagnosis can be difficult, and while numerous categorization criteria have been proposed, their value in the clinical situation is still debatable.

SLE management is controlled by organ system involvement, and despite various medicines that have been demonstrated to be effective in the treatment of SLE, the disease still poses a high morbidity and mortality risk in patients [3]. SLE affects the immune system, thus reducing the body's ability to prevent and fight infection. In addition, many of the drugs used to treat SLE also suppress the function of the immune system, thereby further depressing the ability to fight infection.

The most common infections involve the respiratory tract, urinary tract, and skin and do not require hospitalization if they are treated promptly. Other opportunistic infections, particularly Salmonella, herpes zoster, and Candida infections, are more common in patients with SLE because of altered immune status.

The patient with lupus often has special nutritional needs related to medical conditions that may arise during the course of the disease. These conditions include steroid-induced osteoporosis, diabetes, cardiovascular disease, and kidney disease. Complications of lupus can be serious, even life threatening [4-5].

The present study was undertaken to assess the serious infections in SLE patients, type and site of infection, responsible microorganisms, patient characteristics and the relationship between the duration of immunosuppressant drugs like DMARDS (Disease modifying anti-rheumatic drugs) and the development of infections in SLE, and factors associated with poor drug administration outcomes.

MATERIALS AND METHODS

This observational study was conducted in total 60 SLE patients who visited the Rheumatology/Dermatology OPD and fulfilling SLICC criteria 2012 getting admitted to medicine, dermatology ward or ICU during a period of 18 months. Patients with age below 12 years, who discharged against medical advice, patients with nosocomial infections and who unwilling to participate in the study were excluded.

The relevant data like demographics (name, age, sex. etc.), presenting clinical details about the SLE related and infection related characteristics, detailed examination findings including disease activity by SLEDAI scoring system and physical assessment findings, past illness history and previous drug details were collected in study proforma.

The infections for which patients admitted were diagnosed according to the standard definitions of respective illnesses. However, infection diagnosed by means of positive cultures or compatible clinical features with supportive other evidence of infection and response to antibiotic therapy in cases of negative cultures. The details of the treatment for SLE including immunosuppressive drugs were noted for their cumulative doses, total duration etc. Also, the organ system affected in infections were noted.

Various clinical tests included a complete blood count, urine routine microscopy, blood culture, urine culture, other fluid cultures, and SLE-related serological studies. In addition, imaging investigations such as X-rays, CT scan reports, and other investigations were carried out. Microbiological data were also gathered as culture-positive proved cases or clinically diagnosed cases with suitable supporting laboratory evidence.

Treatment-related data were obtained from patient case reports, including antibiotic dosage, duration of antibiotics taken, and whether antibiotics were given before or after obtaining a microbiological sample for culture. The outcomes of the cases were reported as either death, complete recovery, or recovery with sequelae.

OBSERVATIONS AND RESULTS

Total of 60 SLE patients were studied within the range of 12-80 years of age. Majority of patients belong to age group of 20-30 years with

female predominance (83.3%). Skin system involvement (53.3%) was found to be commonest followed by genitourinary involvement (48.3%). Based on culture positivity urinary tract was most common site of infection (41.66%) followed by respiratory tract (35%). Bacteria were the commonest isolated organism for infection among patients of SLE. In 33.5% of patients' organisms could not be isolated as shown in table 1.

Table 1: Demographic data, systemic manifestations, type and site of infection

Parameters		No. of patients	Percentage
Age groups (years)	13-20	17	28.33
	21-30	23	38.33
	31-40	10	16.66
	41-50	09	15.00
	51-60	01	1.66
	>60	00	0.0
Sex	Female	50	83.3
	Male	10	16.7
System Involved (Systemic manifestations)	Skin involvement	32	53.3
	Genitourinary system	29	48.3
	Respiratory system	24	40.0
	Musculoskeletal system	16	26.6
	Nervous system	10	16.7
	Gastrointestinal System	04	6.7
Site of infections Based on culture positivity	Urinary tract infection	25	41.66
	Respiratory infection	21	35.0
	Skin infection	08	13.35
	Gastrointestinal infection	02	3.33
	CNS infection	02	3.33
	Haematological infection	02	3.33
Infections based on organisms	Bacteria	28	46.6
	Virus	10	16.6
	Fungus	02	3.3
	Not isolated	20	33.5

Table 2 shows 100% incidence of infections among users of rituximab, MPS and cyclosporine. Among users of cyclophosphamide 80% had infections. Association of daily dose of prednisolone with culture positivity which signifies that higher dose of prednisolone associated with higher culture positivity rate. However, no association was found between use of HCQ and culture positivity.

Table 2: Association between prevalence of infection and immunosuppressant used

Drug used		No. of patients	Prevalence of infection	% Of infection
Prednisolone		56	36	65.4
Cyclophosphamide		10	08	80.0
Azathioprine		05	03	60.0
MPS		02	02	100.0
Cyclosporine		01	01	100.0
Rituximab		01	01	100.0
MMF		00	00	0.0
Drugs		No. of patients	Culture positivity	Percentage
Use of HCQ	HCQ	47	22	46.80
	No HCQ	13	06	46.15
Prednisolone dose mg/day	Below 10	42	18	42.85
	Above 10	18	12	66.0

The incidence of associated urinary tract infection (UTI) was maximum (25; 41.6%), followed by lower respiratory tract infection (LRTI) (10; 16.6%), and upper respiratory tract infection (URTI) (9; 15%) as depicted in figure 1.

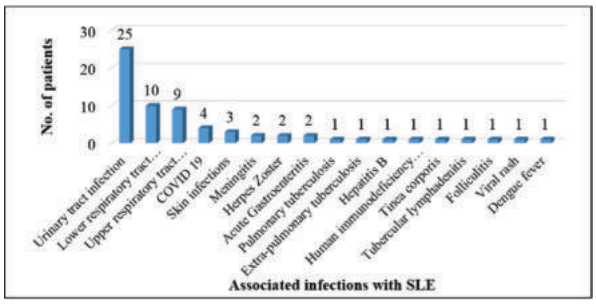

Figure 1: Distribution of cases based on associated Infections with SLE

Among culture positive cases gram negative bacteria contribute 22 (78.5%) and gram positive contributes 6 (21.5%).

Figure 2 shows among all culture positive cases in study population, E. coli contributes most (10; 35.9%) followed by Klebsiella Pneumonae (5; 17.8%), Staph. Aureus (4; 14.4%), and Pseudomonas Aeruginosa (3; 10.7%).

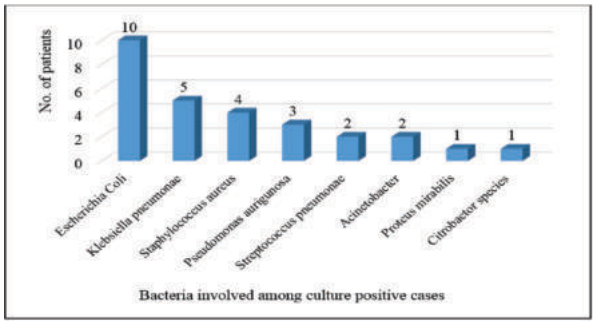

Figure 2: Bacteria involved among culture positive case

Among urine cultured positive cases E. coli contributes most (64.4%) whereas among blood cultured organisms, Streptococcus Pneumonae, Proteus Mirabilis, Klebsiella Pneumonae, Pseudomonas Aurigunosa, Acinetobactor, E.Coli each contributes 1(14.3%) while among other fluid positive cultures, Staphylococcus Aureus contributes most (37.5%) followed by Klebsiella Pneumonae (25%) as shown in table 3.

Table 3: Distribution of patients based on urine, blood, and other fluid cultured organisms

Cultured organisms		No. of patients	Percentage
Urine cultured organisms	Escherichia Coli	09	64.4
	Klebsiella pneumonae	02	14.3
	Pseudomonas aurigunosa	01	7.1
	Yeast	01	7.1
	Citrobactor species	01	7.1
Blood cultured organisms	Streptococcus pneumonae	01	14.3
	Staphylococcus aureus	01	14.3
	Klebsiella pneumonae	01	14.3
	Pseudomonas aurigunosa	01	14.3
	Acinetobactor	01	14.3
	Proteus mirabilis	01	14.3
	Escherichia coli	01	14.3
Other fluid cultured organisms	Streptococcus pneumonae	01	12.5
	Staphylococcus aureus	03	37.5
	Klebsiella pneumonae	02	25.0
	Pseudomonas aurigunosa	01	12.5
	Acinetobactor	01	12.5

In study population 37 (62%) patients have high SLEDAI score (11 and above) and 23(38%) patients have low SLEDAI score (1 to 10).

High severity of SLE based on (SLEDAI≥20) was found to be associated with 22.2 % mortality and 44.4% morbidity. (Recovery with sequelae) Moderately high severity i.e. (SLEDA score -11to19) was associated with 4.8% mortality and 23.8% morbidity. The outcomes were much better in Moderate grade (SLEDAI score- 6 to 10) and Mild (SLEDAI score-1 to 5) with 87.5% and 80% recovery rate, respectively (p=0.029), (Table 4).

Table 4: Outcome, and severity of SLE based on SLEDAI Cross tabulation

Final outcome	High (SLEDAI ≥20)	Moderatel y high (SLEDAI 11-19)	Moderate (SLEDAI 6-10)	Mild (SLEDAI 1-5)	Total	P value
Death	4 (22.2%)	01 (4.8%)	00 (0.0%)	00 (0.0%)	05 (8.3%)	0.029
Recover ed complet ely	06 (33.3%)	15 (71.4%)	14 (87.5%)	04 (80.0%)	39 (65.0%)	
Recover ed with sequelae	08 (44.4%)	05 (23.8%)	02 (12.5%)	01 (20.0%)	16 (26.7%)	
Total	18 (100%)	21 (100%)	16 (100%)	05 (100%)	60 (100%)	-

Out of 60 patients 50(84%) recovered completely, 5(8%) recovered with sequelae and death occur in 5(8%) cases, (Figure 3). 18 (30%) patients require below 5 days course of antibiotics, 35(58%) require 6-10 days, 6(10%) require 11-15 days of antibiotics, and 1(1.6%) require 15 days of antibiotics.

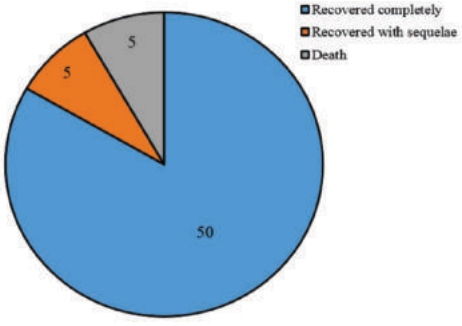

Figure 3: Distribution of cases based on outcome

DISCUSSION:

In the present study, infections in SLE patients were common in young age group of 20 to 30 years with a mean age of 27.5 years, with female predominance (83.3%) which is correlated with the study conducted by Santhanam et al [6]. In context of systemic manifestations, skin involvement when considered separately was found to be commonest followed by genitourinary involvement. Gastrointestinal system was least involved. This finding is comparable with the study done by Paudyal BP et al [7] and Miah et al [8]. Based on culture positivity urinary tract was most common site of infection (41.66%) followed by respiratory tract (35%) followed skin (13.35%) which is correlated with the study done by Dorgham et al [9].

During the study, we administered prednisolone at the frequency of 56 (95%), where the dose ranged from 10mg/day to more than 40mg/day. Most of the patients (42 cases) were taking lower dose of Prednisolone that was less than 10mg/day of dose, 13 patients received prednisolone dose between 11 to 39 mg/day and only 5 patient was given more than 40 mg/day of dose. It was found that among 42 cases on low dose prednisolone, 18 (42.85%) cases had culture positive infection. Among 18 patients receiving prednisolone more than 10mg/day, 12 had culture positive infection (66%). These findings are similar to study conducted by Dixon et al [10]. Whereas 47 patients were on HCQ among them 22 (46.80%) had culture positive infection and among 13 non-users of HCQ 6(46%) had culture positive infection which was similar to study conducted by Zonana –Nacach et al [11]. Apart from prednisolone, and HCQ, another drug was also administered to the patients of SLE. The drugs used in current study were azathioprine -5, Cyclophosphamide-10, cyclophosphamide-1, rituximab-1, MPS-2, MMF-0.

Incidence of infections in patients taking above medications was observed and it was found that 65.4% of patients on prednisolone had infection, 60% patients on azathioprine had infection, 80% patients on cyclophosphamide had serious infection. Serious infection found in all patients receiving rituximab, MPS and Cyclosporine. These findings are correlated with the previous studies [12, 13].

Associated infections in SLE were UTI, it was maximum i.e., 41%, followed by LRTI 10(16.6%) and URTI 9(15%). Incidence of Skin infections -3(5%). Herpes zoster- acute gastroenteritis and meningitis were 2(3%) for each. Pulmonary TB, extra pulmonary TB, tubercular lymphadenitis, HIV, Hepatitis B, tinea corporis, and folliculitis shows frequency of 1 (1.6%) each. It has recently been reported that even COVID-19 infection triggered the development of SLE [14]. However, among the patients we encountered 56 of them were COVID19 negative and only 4 were positive. These findings are comparable with the other studies [15, 16].

Bacteria were the commonest isolated organism for infection among patients of SLE (46.6%) followed by virus (16.6%) and fungus (3.3%). In 20 patients (33.5%) organisms could not be detected. This is similar to the study conducted by Dorgham et al [9], Luitjen et al [17] and Torres-Ruiz J et al [18]. The most common bacteria responsible for infections was E. Coli 10 (35.9%) followed by Klebsiella pneumonae-5(17.8%), Stphylococcus aureus 4(14.4%), Pseudomonas aurigunosa-3(10.7%), Streptococcus pneumonae-2(7.1%), Acinetobactor-(2%), Proteus Mirabilis1(3.5%), Citrobactor Species-1(3.5%). Among all culture positive bacteria 22(78.5%) were gram positive and 6(28.4%) were gram negative. Similar findings are reported in Torres-Ruiz et al study [18].

In the present study, results were divided based on their severity, i.e., high (SLEDAI≥20), Mild (SLEDAI between11-19), moderate (SLEDAI between 6-10) and moderately high (SLEDAI between 1-5). Where, the number of patients with high SLEDAI score were 18, among them 4 patients died, 6 recovered completely and 8 recovered with sequelae. On the other hand, 21 patients with mild to moderate SLEDAI score survived and where the recovery rate in moderate SLEDAI score were high (87.5%) as compared mild (80%). At last, out of 21 patients with moderately high SLEDAI score 20 recovered, of them 15 recovered completely and 5 recovered with sequelae. Within those group we have reported one death as well. When pearson's chi squared, test was applied to find degree of association between SLEDAI score and severity/poor outcome, p value was found to be <0.029, indicating strong association. These results are comparable with the study done by Noel et al [19].As the outcome of the study and treatment, 50 (83%) patients completely recovered, and 5 (8%) deaths were reported. Apart from this, 5 patients recovered with sequelae which is in accordance with the earlier studies [8, 20, and 21]

CONCLUSION:

SLE is a multisystem disorder affecting predominantly young females. Skin involvement was commonest followed by genitourinary involvement. Urinary tract was the most common anatomical site involved followed by respiratory tract. Bacteria were the most common isolated organism and gram-negative bacteria were more common. Escherichia coli followed by Klebsiella pneumonae were the most common bacteria isolated. Significant association was found between SLEDAI score and severity /poor outcome in patients of SLE with infections. Risk factors associated with infections include use of prednisolone more than 10 mg/day, use of cyclosporine/ rituximab/ MPS and cyclophosphamide. Hence, management of SLE needs vigilance for infection and judicious use of immunosuppressive drugs.

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