



The Brazilian Journal of INFECTIOUS DISEASES


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Letter to the editor

Report of multidrug resistant bloodstream bacterial infections in systemic lupus erythematosus patients in Southern India



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ARTICLE INFO

Article history:

Received 20 April 2020

Accepted 24 July 2020

Available online 7 August 2020

Dear Editor,

Systemic lupus erythematosus (SLE) is an autoimmune disease resulting in inflammation-mediated multiorgan damage. In SLE patients, bacteria cause a higher rate of infections than viruses and/or fungi. Among SLE patients, bacterial infections is responsible for about 20–55% of death.^{1,2} Bacteremia frequently occurs in this population due to regular and continued usage of glucocorticoids and immunosuppressive agents for their treatment.³ In this study, we isolated the pathogenic bacteria from blood samples collected from the SLE patients in Southern India and they were analyzed for their resistance profile to standard antibiotics. A total of 100 blood samples were collected from SLE patients. Isolated bacterial cultures were further subjected to antibiotic sensitivity assay or antimicrobial resistance (AMR) profiling using Kirby-Bauer Disk Diffusion method according to CLSI guidelines.⁴ Ethical

approval for this study was obtained from the Institutional Review Board of Madras Medical College, Chennai, India.

Age and sex-wise distribution of SLE patients revealed that about 91% of the infections were among females and only 9% were in males. Among the various age groups, 49% were in the age group of 21–30 years, followed by 22% in 31–40 years, 17% in 10–20 years, 10% in 41–50 years and 2% in 51–60 years. Among SLE patients, butterfly rash were recorded in 26% of the patients followed by a discoid rash in 41%, Reynaud's phenomenon in 37%, fever in 31%, thick red, scaly red patches in 46%, hemolytic anemia in 18%, thrombocytopenia in 28%, arthritis in 54%, photosensitivity in 49%, oral ulcer in 24%, and alopecia in 16%. The SLE patients were treated with the following immunosuppressive drugs viz. prednisolone, cyclophosphamide, hydroxychloroquine, glucocorticoids, and azathioprine. In this study, a total of 50 SLE patients had bloodstream infections and among them 45 patients had bacterial infection and five patients had fungal infection.

The antibiotic susceptibility profile was carried out only for the bacterial isolates. *Escherichia coli* isolated from blood specimens showed 100% resistance to ampicillin, ceftazidime, cefotaxime, cefuroxime, piperacillin, gentamicin, followed by

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<https://doi.org/10.1016/j.bjid.2020.07.005>

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Table 1 – Antibacterial susceptibility pattern of bacterial isolates from blood samples of SLE patients.

	Name of the Bacteria	Interpretation	Antibacterial drugs															
			AK	AMP	C	CX	DO	IPM	CAZ	PTZ	CTX	CXM	CN	CPM	CZ	SXT	AZ	AUG
1	<i>Enterococcus spp.</i>	Resistant	0	7	1	1	0	0	1	0	0	-	0	0	0	7	1	3
		Intermediate	0	0	0	1	0	0	3	0	0	-	0	0	2	0	2	0
		Sensitive	7	0	6	5	7	7	3	7	0	-	7	7	5	0	4	4
2	<i>Escherichia coli</i>	Resistant	0	7	1	0	0	0	7	7	7	7	7	6	6	6	2	6
		Intermediate	3	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0
		Sensitive	4	0	6	7	6	7	0	0	0	0	0	0	1	1	4	1
3	<i>Salmonella spp.</i>	Resistant	0	5	0	1	0	0	0	0	-	-	-	-	-	-	-	-
		Intermediate	1	0	0	0	0	0	3	0	-	-	-	-	-	-	-	-
		Sensitive	4	0	5	4	5	5	2	5	-	-	-	-	-	-	-	-
4	<i>Staphylococcus aureus</i>	Resistant	0	0	0	0	0	0	0	0	-	-	-	-	-	-	0	-
		Intermediate	0	1	0	0	0	0	0	0	-	-	-	-	-	-	1	-
		Sensitive	3	2	3	3	3	3	3	3	-	-	-	-	-	-	2	-
5	<i>Proteus spp.</i>	Resistant	0	5	0	1	0	0	1	0	5	-	5	-	-	-	-	5
		Intermediate	1	0	0	1	0	0	1	0	0	-	0	-	-	-	-	0
		Sensitive	4	0	5	3	5	5	3	5	0	-	0	-	-	-	-	0
6	<i>Klebsiella pneumoniae</i>	Resistant	0	6	0	0	0	0	1	5	4	6	6	4	0	6	0	5
		Intermediate	1	0	0	0	1	0	1	0	0	0	0	2	4	0	0	0
		Sensitive	5	0	6	5	5	6	4	1	2	0	0	0	2	0	6	1
7	<i>Streptococcus pneumoniae</i>	Resistant	1	1	0	1	1	0	1	0	-	-	-	-	-	-	-	-
		Intermediate	0	0	0	0	1	0	0	1	-	-	-	-	-	-	-	-
		Sensitive	3	3	4	3	2	4	3	3	-	-	-	-	-	-	-	-
8.	<i>Enterobacter spp.</i>	Resistant	0	6	0	1	0	0	1	0	-	-	-	-	-	6	-	-
		Intermediate	0	0	1	0	0	0	4	0	-	-	-	-	-	0	-	-
		Sensitive	6	0	5	5	6	6	1	6	-	-	-	-	-	0	-	-

AK-Amikacin; AMP-Ampicillin; C-Chloraphenicol; CX-Cefoxitin; DO-Doxycycline; IPM Imipenem; CAZ-Ceftazidime; PTZ-Piperacillin/Azobactam; CTX-Cefotaxime;CXM-Cefuroxime;CN-Gentamicin;CPM-Cefepime;CZ-Cefazolin; SXT-Co-trimaxozole; AZ-Azithromycin; AUG-Amoxicillin/Clavulanic acid.

86% to amoxicillin/clavulanic acid, co-trimoxazole, cefepime and cefazolin (Table 1). *Klebsiella pneumoniae* showed 100% resistance to ampicillin, gentamicin, co-trimoxazole, cefuroxime followed by 83.3% to piperacillin, amoxicillin/clavulanic acid, and 66.7% to cefepime and cefotaxime. *Salmonella* spp. exhibited 100% resistance to ampicillin, enterobacter showed 100% resistance to ampicillin, co-trimoxazole, and 100% of *Proteus mirabilis* exhibited resistance to ampicillin, cefotaxime, amoxicillin/clavulanic acid, and gentamicin. Majority of the *Staphylococcus aureus* isolates showed resistance against penicillin (83.3%) followed by azithromycin (67%) (Table 1). Molecular screening for β -lactamase producing drug resistance genes showed that three isolates of *E.coli* were positive for *bla*_{TEM}, two isolates of *E.coli* for *bla*_{CTX-M}, and one isolate of *K. pneumoniae* showed positive for *bla*_{TEM}, and *bla*_{CTX-M}, and one isolate of *P. mirabilis* showed positive for *bla*_{TEM}.

The bacteria like *E. coli*, *S. aureus* and *Salmonella* spp. causes bloodstream infections in SLE patients and *Salmonella* spp. was the most common and major etiology among them.^{3,5} *Streptococcus pneumoniae* caused about 10.3% of the bacteremia in SLE patients and about 54.5% of the infections caused by the microorganisms develop into severe SLE flare.⁶ In this study, Gram-negative bacteria like *E. coli* and *Salmonella* spp. were the major medically important etiology causing the majority of bloodstream infections. In case of Gram-positive bacteria *Enterococcus* spp. was the major causative agent with very high infection rate followed by *S. aureus* and *S. pneumoniae*. Reports of drug resistance among bacteria causing bloodstream infections in SLE patients are scarce. This study highlights drug resistant bacteria causing bloodstream infections among SLE patients which might be a risk factor and complicate the clinical management of these patients with available antibiotics. Bloodstream infections caused by drug resistant bacteria in SLE patients might prolong hospital stay, increase treatment cost, i.e., out-of-pocket expenditure for the treatment/management of secondary infections and may also

increase the severity of the disease condition. The need of the hour is to establish rapid diagnosis and continued surveillance system to identify the causative bacterial agent. Adequate antibiogram would be helpful in implementing an appropriate therapeutic option for mitigating the drug resistant bloodstream infections in SLE patients.

Conflict of interest

The author declares no conflicts of interest.

REFERENCES

1. Cervera R, Khamashta MA, Font J, et al. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: A comparison of early and late manifestations in a cohort of 1,000 patients. *Medicine (Baltimore)*. 2003;82:299-308.
2. Fessler BJ. Infectious diseases in systemic lupus erythematosus: risk factors, management and prophylaxis. *Best Pract Res Clin Rheumatol*. 2002;16:281-91.
3. Marcos M, Fernandez C, Soriano A, et al. Epidemiology and clinical outcomes of bloodstream infections among lupus patients. *Lupus*. 2011;20:965-71.
4. Clinical and Laboratory Standards Institute (CLSI). Performance standards for Antimicrobial Susceptibility Testing. Wayne, PA: Twenty First Informational Supplement S21. M100, CLSI; 2012.
5. Goldblatt F, Chambers S, Rahman A, Isenberg DA. Serious infections in British patients with systemic lupus erythematosus: Hospitalisations and mortality. *Lupus*. 2009;18:682-9.
6. Ruiz JJ, Barrera-Vargas A, Ortiz-Hernandez R, Alcocer-Varela J, Gomez-Martin D. Bloodstream Infections in Systemic Lupus Erythematosus Patients Are Associated with Severe Lupus Flares. *Arthritis & Rheumatology*. 2015;67:2230-1.