

ORIGINAL ARTICLE

Detection of Bacterial Infection in Systemic Lupus Erythematosus Patients and their Antibacterial Susceptibility Pattern in Mansoura University Hospital

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ABSTRACT

Key words:

Systemic lupus erythematosus, bacterial infection, antibacterial susceptibility

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that affects the majority of organs and tissues. SLE flares and bacterial infections are major causes of death in these patients and detection of bacterial infections in them is essential due to different therapy and their clinical manifestations can be similar. **Objectives:** The objectives of this research were to identify microorganisms causing bacterial infection in SLE patients and their antimicrobial susceptibility pattern in comparison with bacterial infections in patient with other medical illness in Faculty of Medicine, Mansoura University. **Methodology:** Urine, blood and other specimens were collected from SLE and non- SLE patients clinically suspected of bacterial infection.. The samples collected were cultivated on blood agar, MacConkey agar, chocolate agar, Sabouraud dextrose agar media (SDA), whereas urine specimens were cultivated on cysteine lactose electrolyte deficient (CLED) and blood samples were inoculated in blood culture bottles. Isolated bacteria were identified by colonial morphology, Gram stained films and biochemical reactions. Antibacterial susceptibility pattern was determined by disc diffusion method. **Results:** Urinary tract infection (UTI) was the most common bacterial infection among SLE patients (55%) while bacterial pneumonia was the most common infection in non-SLE patients (50%). Gram negative bacteria were 80.76% of culture isolates in SLE patients while Gram positive bacteria were isolated at a rate of (19.23%). *Escherichia coli* were the most predominant organism (26.92%). Gram negative bacteria showed highest sensitivity to Piperacillin-tazobactam while Gram positive organisms exhibited 100% sensitivity for Ciprofloxacin, Cefuroxime, Gentamycin and Imipenem. **Conclusion:** the high morbidity and mortality rates associated with bacterial infections in SLE and its similarity with lupus flare, make accurate detection is very important in order to offer successful treatment and ensure better patient outcome.

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is defined as a rheumatic disease due to autoimmune reaction. It is associated with extensive inflammation, with all body organs or systems affection. The prevalence has been found to be more common in females particularly at the age of 15-40 years¹. A representative study for prevalence of SLE in Egypt was conducted from January 2011 to April 2014 on 939 patients in Assiut University Hospital, SLE prevalence was 14.3%².

The leading reasons of mortality in SLE patients are major disease flare leading to organ failure, infections, and cardiovascular system affection. Mortality rate in SLE patients is 3-5 times higher than general population³.

Increased incidence of infection in SLE patients is attributed to the usage of immunosuppressive drugs and complications of vital body organs during the pathogenesis of the SLE disease^{4,5}.

Loss of integrity of epithelial barriers in SLE patients because of rashes, ulcers, and cutaneous wounds can contribute to access of infectious microorganisms to the body. It has been shown that there is gathering of T gamma-delta cells in normal and abnormal skin of SLE patients in comparison with the skin of healthy people⁶. Gathering of T gamma-delta cells leads to skin epithelial breakdown, therefore increasing incidence of infection⁷.

In addition, increased risk of infections in SLE patients with mannose-binding lectin (MBL) deficiency is due to impaired stimulation of the complement

system by MBL thus defective clearance of microorganisms⁸. Furthermore, some polymorphonuclear cell (PMNs) abnormalities for example abnormalities in chemotaxis, steps of phagocytosis and cytokine secretion (particularly IL-8), are observed in SLE patient⁹.

METHODOLOGY

Ethics approval:

The research was approved by the Faculty of Medicine, Mansoura University Institutional Research Board. Participants gave written informed permission to use their specimens in diagnostic studies.

Study design:

This study was a prospective one, carried out over a period of 24 months from July 2016 to June 2018 on adult patients who attended special Outpatient Clinics or were admitted to the Inpatient Department in Faculty of Medicine, Mansoura University.

Study population:

This study involved twenty febrile SLE patients with positive bacterial infection culture and twenty febrile non SLE patients with verified bacterial infection cultures.

Data collection:

The following data were collected: demographic characteristics of the patients included age and sex, Clinical diagnosis on hospital admission, invasive devices such as (central venous line, intercostal tubes and urinary catheters) and prescribed antibiotics as regard type and duration.

Clinical samples:

Blood and urine were collected routinely from all patients. In addition sputum, wound and vaginal swabs were obtained from patients according to body sites suggestive of infection. All specimens were from febrile patients before antibiotic therapy has been started

Microbiologic studies:

Samples were immediately transported to the Microbiology Diagnostics and Infection Control Unit (MDICU) laboratory of the Department of Medical Microbiology and Immunology, Faculty of Medicine, Mansoura University, for further processing. Sputum, vaginal and wound specimens were cultivated on blood agar, MacConkey's agar, chocolate and Sabouraud dextrose agar media (SDA), whereas urine specimens were cultivated on cysteine lactose electrolyte deficient (CLED) media and SDA. Blood samples were cultured on blood culture bottles. Isolated colonies were identified according to colony characteristics, Gram stained films and different biochemical reactions (catalase test and coagulase test for Gram positive organisms; citrate utilization, kligler iron agar, urease test, lysine iron agar, oxidase test and motility indole ornithine agar for Gram negative organisms).

Antibiotic Susceptibility Testing:

The disk diffusion method was applied to the isolated bacteria according to the guidelines of Clinical and Laboratory Standards Institute (CLSI)¹⁰.

RESULTS

Site of bacterial infection in SLE patients versus non-lupus patients

The bacteria-infected group in SLE patients included 11 cases with UTI (5 complicated with sepsis), 8 with bacterial pneumonia (2 with sepsis), 2 with catheter related blood stream infection (CRBSI), 2 with wound infection and 1 with bacterial vaginitis. Three cases concurrently had bacterial pneumonia and UTI (1 with sepsis) and one had bacterial vaginitis and urinary tract infection simultaneously. Totally, 9 patients had sepsis as illustrated in table 1.

Table 1: Site of bacterial infection in SLE patients group

Site of infection	Number (20)	%
UTI	11	55
Blood stream infection	9	45
Bacterial pneumonia	8	40
Catheter related blood stream infection (CRBSI)	2	10
Wound infection	2	10
Bacterial vaginitis	1	5

In contrast, bacterial pneumonia was the commonest in non SLE bacteria-infected group which included 10 cases (3 with sepsis). UTI occurred in 9 cases and 2 cases complicated with sepsis. Other bacterial infections included 3 with wound infection and 2 with CRBSI. There were four cases of bacterial pneumonia and UTI concurrently (3 with sepsis). Totally, 7 patients had sepsis as demonstrated in table 2.

Table 2: Site of bacterial infection in non-lupus patients group

Site of infection	Number (20)	%
Bacterial pneumonia	10	50
UTI	9	45
Blood stream infection	7	30
Wound infection	3	15
Catheter related blood stream infection	2	10

Frequency of isolated bacteria in SLE patients versus non-lupus patients

Polymicrobial infection was detected only in 2 cases of SLE patients while in non-lupus patients was detected in 4 cases and monomicrobial infection was

the commonest in both SLE and non-lupus patients (figure1; 2).

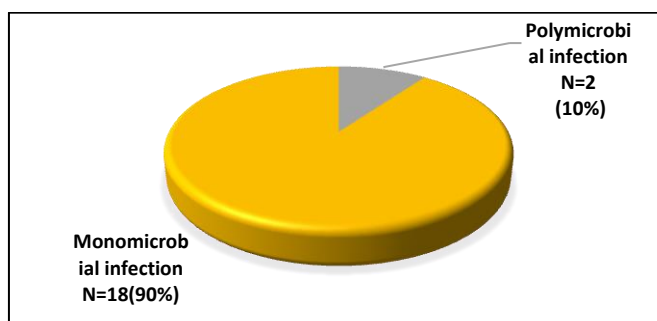


Fig. 1: Frequency of monomicrobial vs polymicrobial infection_in SLE patient group

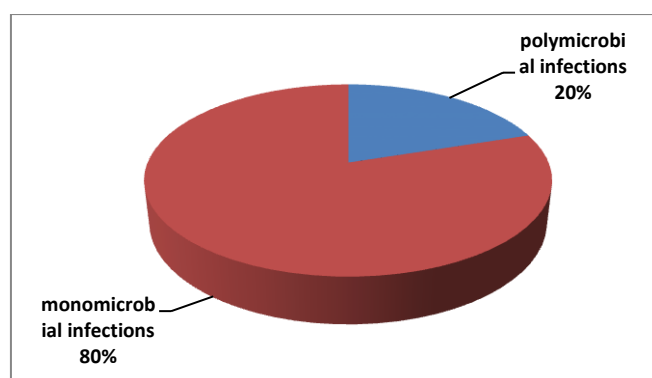


Fig. 2: Frequency of monomicrobial vs polymicrobial infection in non-lupus patient group

Gram negative bacteria were 80.77% of culture isolates in SLE patients and were 54.17% in non-lupus patients whereas Gram positive bacteria at a rate of isolation (19.23%) in SLE patients versus (45.83%) in non-lupus patients.

In SLE patients, The most frequently isolated bacteria were *E. coli* (26.92%), *Acinetobacter*

baumannii, (19.23%), *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* (11.54% each), *Proteus mirabilis* (7.69%), *Staphylococcus aureus* (7.69%), with equal isolation of *Citrobacter* spp, *Streptococcus pneumoniae*, *Methicillin-resistant Staphylococcus aureus (MRSA)*, and *Enterococci* spp (3.85%) (figure3).

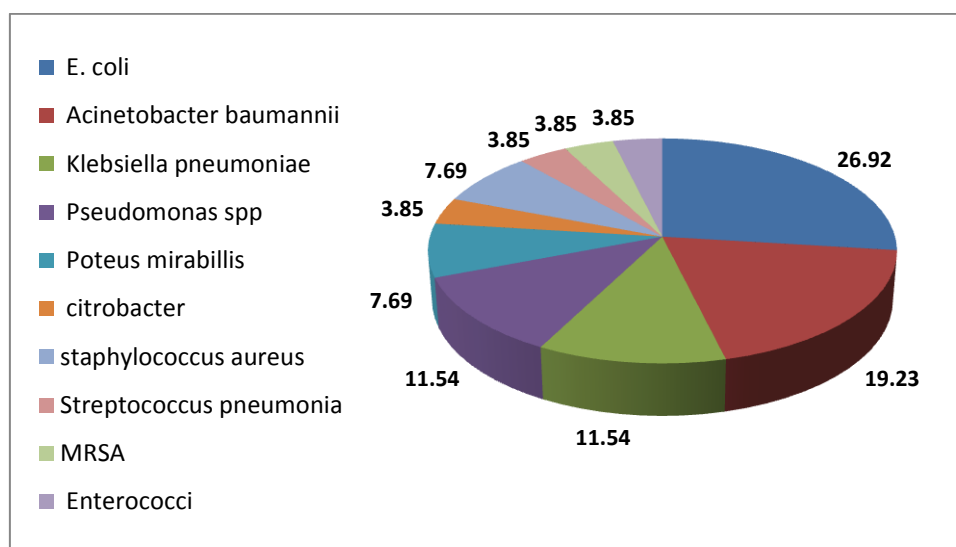


Fig. 3: Frequency of isolated bacteria in SLE patients group

In non-lupus patient, the most commonly isolated organisms were *Staphylococcus aureus* (25%), *E. coli* (20.83%), *Klebsiella pneumoniae* (16.67), *Streptococcus pneumoniae* (12.5%) and *Pseudomonas*

aeruginosa (9.09%), with equal isolation of *Proteus mirabilis*, *Citrobacter* spp, coagulase negative staphylococci, and *Enterococci* spp (4.17%) (Figure 4).

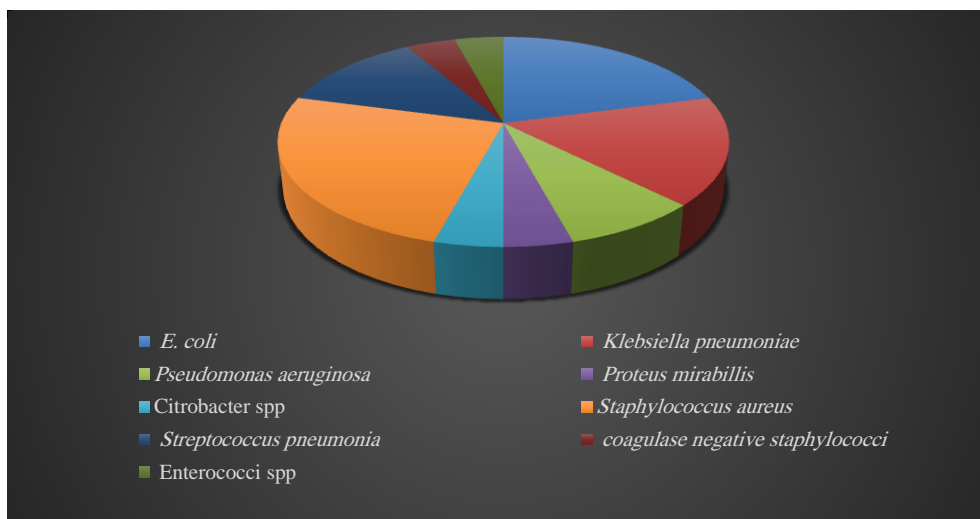


Fig. 4: Frequency of isolated bacteria in non-lupus patients group

Antibiotic susceptibility pattern of isolated organisms in SLE patients in comparison with that in non-lupus
Gram negative bacteria

As regard antibiotic sensitivity pattern in SLE patients, all Gram negative bacteria had 100% sensitivity to Piperacillin-tazobactam, followed by Imipenem (85.7%), Amikacin (78.6%), Gentamycin (70%), Cefoperazone-sulbactam (62.5%), Cefipime (58.3%), Ciprofloxacin (55.6%), Amoxicillin-clavulanic (50%), Cefoperazone (16.7%), Meropenem (16.7%), Sulphamethoxazole-trimethoprim (12.5%), Cefotaxime (11.1%), Ceftazidime (0%) and Levofloxacin (0%) as shown in figure 5.

(70%), Cefoperazone-sulbactam (62.5%), Cefipime (58.3%), Ciprofloxacin (55.6%) and Amoxicillin-clavulanic (50%). Meanwhile the sensitivity for Cefoperazone and Meropenem was 16.7% for each but Sulphamethoxazole-trimethoprim sensitivity was 12.5%. While, sensitivity rates for Ceftriaxone was 11.1%. Isolates were totally resistant to Ceftazidime and Levofloxacin as shown in figure 5.

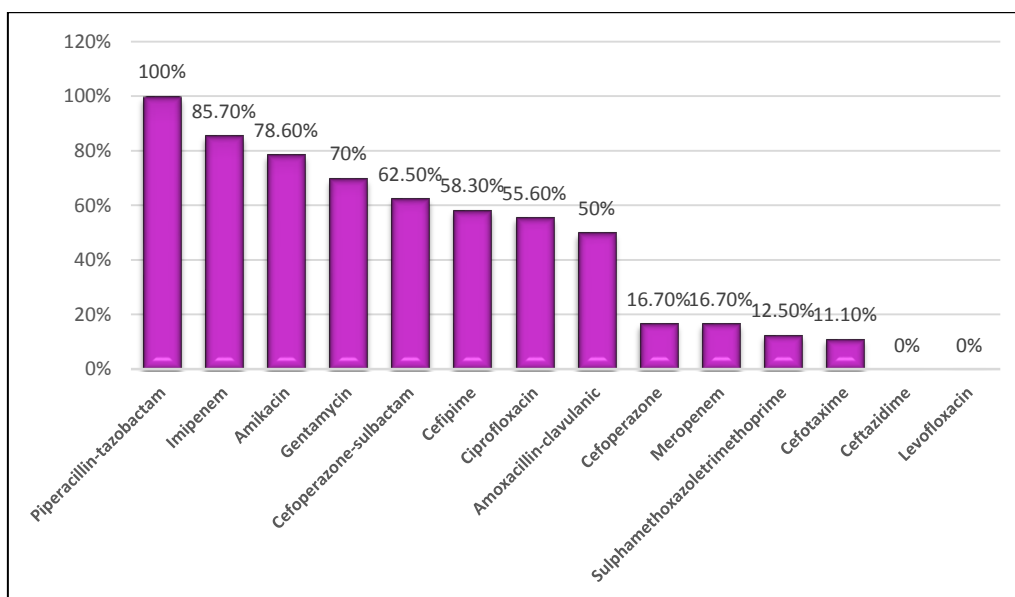


Fig. 5: Antibacterial sensitivity of the isolated Gram negative bacteria in SLE patients group

In non-lupus patients, Gram negative bacteria showed 71% sensitivity to Cefoperazone-sulbactam, followed by Amikacin (66.7%), Ciprofloxacin (60%), gentamycin (50%) and Amoxicillin-clavulanic (44%). Meanwhile for imipenem and Piperacillin-tazobactam, the sensitivity was 33.3% for each and

Sulphamethoxazole-trimethoprim was of lower sensitivity of 16.7%. Cefotaxime was sensitive in 11% of isolated microorganism. Isolates were totally resistant to Cefipime, Meropenem, Cefotaxime, and Levofloxacin as illustrated in figure 6.

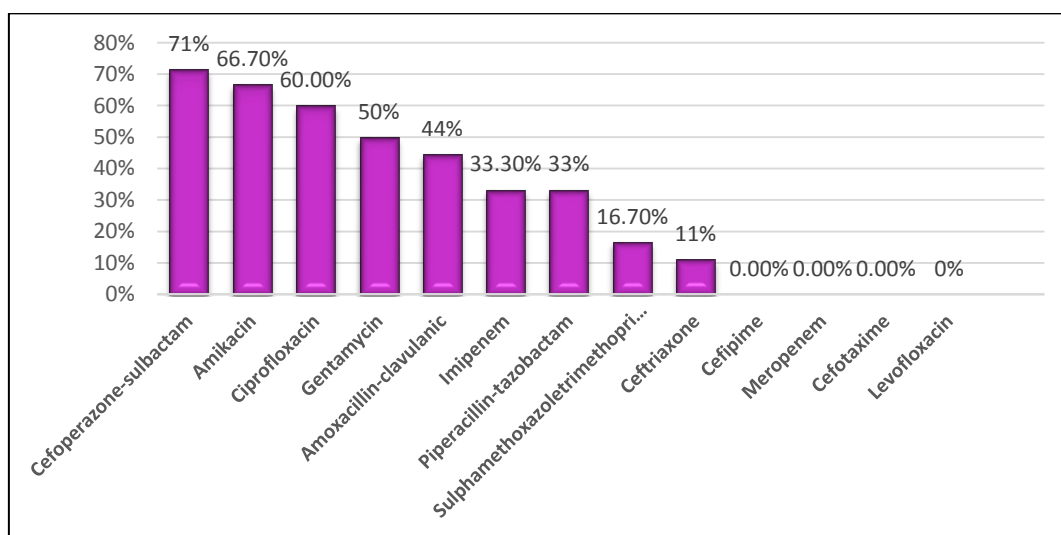


Fig. 6: Antibacterial sensitivity of the isolated Gram negative bacteria in non-lupus patients group

Gram positive bacteria

All isolated Gram positive bacteria in SLE patients exhibited 100% sensitivity for Ciprofloxacin, Cefuroxime, Gentamycin and Imipenem. The sensitivity for Cefoperazone-sulbactam, Ceftriaxone and

Azithromycin were of equal sensitivity (50%), but sensitivity to Cefoxitin and Doxycycline were 12.5% and 11.15% respectively. Isolates were totally resistant to Amoxicillin-clavulanic, Levofloxacin and Clindamycin as illustrated in figure 7.

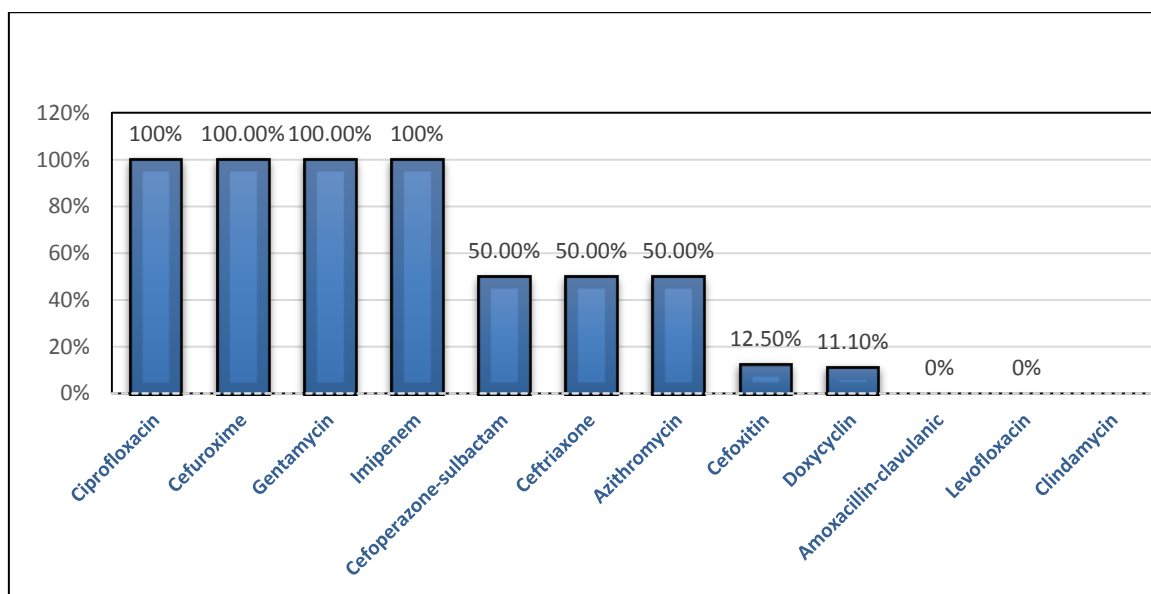


Fig. 7: Antibacterial sensitivity of the isolated Gram positive bacteria in SLE patients group

Finally, the isolated Gram positive bacteria in non-lupus patients exhibited 100% sensitivity for Cefoperazone-sulbactam and Doxycycline followed by Ciprofloxacin (67%), Azithromycin (66.7%),

Clindamycin (50%) and Gentamycin (40%). The sensitivity to Cefoxitin was 11.1%. Isolates were totally resistant to Cefuroxime, Ceftriaxone, Amoxicillin-clavulanic and Levofloxacin as presented in figure 8.

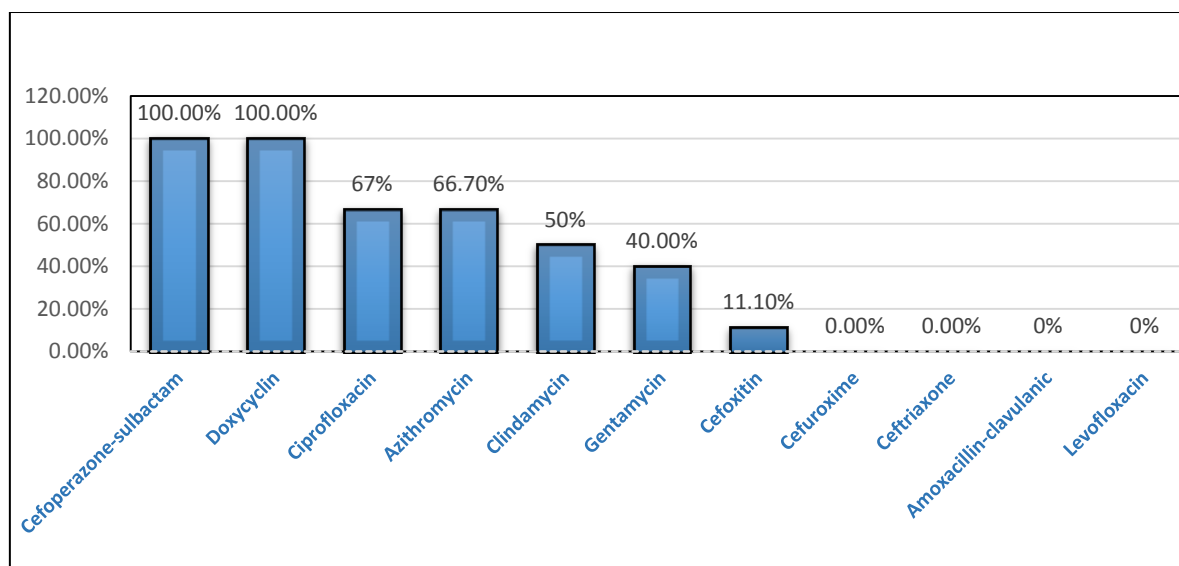


Fig. 8: Antibiotic susceptibility of the isolated Gram positive bacteria in non- lupus patients group

DISCUSSION

Systemic lupus erythematosus (SLE) is the prototype of autoimmune disease, of unknown etiology, although its mechanisms involve genetic, epigenetic and environmental risk factors¹¹. As Mortality rate due to infection in SLE patients is approximately 25%, making it an important cause of death in those patients¹².

The aim of this study was Identification of microorganisms causing bacterial infection in lupus patients and their antimicrobial susceptibility pattern in comparison with bacterial infections in patients with other medical illness. The study was conducted on 20 adult bacterial infected SLE patients and 20 bacterial infected patients with medical diseases other than SLE.

In SLE patients, infections were traditionally regarded as a complication of immunosuppressive treatment, as a recent retrospective cohort study verified¹³. Nevertheless, in the lack of immunosuppressive treatment, 25.9% of serious infections in patients with SLE happen¹⁴ and prior researches have defined disease activity and frequency of flares as autonomous risk variables for infections¹⁵, due to the immunological defects that characterize the illness¹⁶.

The most common site of bacterial infection among SLE patients in our study was UTI (55%). These results

are similar to those reported by^{17,18,19,20} and²¹. They concluded in their research that UTI was the most common bacterial infection. Other studies, however, revealed that bacterial pneumonia was the most common one²²⁻²⁴.

In non-lupus patients, the most common site of bacterial infection in our study was pneumonia (50%). These results are close to those reported by Yang et al.²⁵ who reported that bacterial pneumonia was the most common one (62.5%).

Poly-microbial bacterial infections in SLE patients were isolated in 10% of our research team which was in agreement with Zonana-Nacach et al¹⁷. In contrast, lower rate of 3.2% was reported by Patrick et al²⁴. We speculate this distinction because of our study's small sized number.

The causative microorganisms of bacterial infection in SLE patients are different from one geographical area to another. Gram negative bacteria and Gram positive bacteria were found in 81.18% and 18.18% of Positive results of culture respectively in this study.

Gram negative organisms were the predominant ones in parallel with our finding in studies conducted by another^{17,26,22,24}. In dissimilarity, some trials showed that Gram positive bacteria predominated^{23,27}.

In our study, *E. coli* was the most predominant Gram negative isolate (26.92%) which was in consistent with studies of^{18,19,28,24} who reported that *E. coli* was the Gram negative organism most frequently isolated at a

rate of 13.2, 13.6%, 20.3% and 21.8% respectively. In contrast, *E. coli* was much lower in isolation of 8.7% in another study²⁵.

As for Gram positive bacterial infection in SLE patients in our study, *Staphylococcus aureus* is the most commonly isolated Gram positive bacteria which is close to the results of^{29,24}. In contrast, another study reported the predominance of *Enterococci*²².

As regard bacterial infection in non-lupus patients in our result, *Staphylococcus aureus* was the commonest isolate (25%) which is inconsistent with the work which reported *Streptococcus pneumoniae* as the commonest isolate (25%)²⁵.

The isolated Gram negative bacteria in the present study showed (100%) sensitivity to Piperacillin-tazobactam, followed by Imipenem (85.7%) while the least sensitivity was to Ceftazidime and Levofloxacin (0%).

This sensitivity pattern was similar to that reported by Vasanthi³⁰ who reported sensitivity to Imipenem (100%) and Piperacillin-tazobactam (95.7%). In addition, similar rates of sensitivity of Gram negative bacteria to Imipenem (86.1%) and Piperacillin-tazobactam (66.1%) were reported²⁸.

CONCLUSION

Bacterial infection is very common infection in SLE patients and its detection is very important for correct management of those patients. Urinary tract infection was the commonest infection detected and *E.coli* was the most common isolate in those patients.

- The authors declare that they have no financial or non-financial conflicts of interest related to the work done in the manuscript.
- Each author listed in the manuscript had seen and approved the submission of this version of the manuscript and takes full responsibility for it.
- This article had not been published anywhere and is not currently under consideration by another journal or a publisher.

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