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Bacterial diversity in sepsis patients under ICU care and their antibiotic resistance pattern in Diabetic patients in comparison to non-Diabetic patients with sepsis

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ABSTRACT:

— ***Objective:*** Sepsis and septic shock are the leading cause of morbidity and mortality in both diabetic and non-diabetic patients with a wide diversity of bacteria prevalent in the community. Local data about antimicrobial resistance in both diabetic and non-diabetic patients should be available for proper initiation of empirical therapy. Our aim is to evaluate the spectrum of pathogens causing sepsis and septic shock and their profiles of antimicrobial resistance on a series of diabetic and non-diabetic patients.

— ***Patients and Methods:*** A prospective observational study with 495 participants was conducted targeting the diabetic and non-diabetic patients admitted with sepsis or septic shock in intensive care unit (ICU). Antibiotic sensitivity test was done on each of the isolates and the results of the antibiogram were compared between diabetic and non-diabetic patients. The statistical analysis was done by Chi-Square test, Fisher's exact test using statistical product and service solutions known as statistical package for the social sciences (SPSS), 17.0 version (Chicago, IL, USA).

— ***Results:*** The most common isolated organism was *Klebsiella* followed by *Escherichia coli*, *Staphylococcus, Acinetobacter* and *Enterococcus* in both diabetic and non-diabetic patients. Highest sensitivity was seen for tigecycline and colistin whereas highest resistance was seen for cephalosporin, fluoroquinolones and carbapenems in both diabetic and non-diabetic patients. Statistically significant results were seen for sensitivity for Trimethoprim-sulfamethoxazole for *Acinetobacter* and *Escherichia coli*. Statistically significant results for carbapenem, beta Lactam + beta Lactamase Inhibitor, cefepime were observed for *Klebsiella* and for teicoplanin and vancomycin was observed for *Enterococcus*.

— ***Conclusions:*** This study helps to understand the diversity of bacteria prevalent in community and formulate a better empirical antibiotic usage policy with proper implementation of antibiotic stewardship in a better way. Empirical antibiotic therapy should be prescribed only after performing antimicrobial susceptibility testing in order to obtain a better outcome.

— ***Keywords:*** Sepsis, Bacterial diversity, Resistance pattern, Diabetes, Gram negative bacteria, Gram positive bacteria.

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INTRODUCTION

Sepsis and septic shock, with subsequent multi-organ failure, are the leading causes of mortality in intensive care units[1]. Sepsis accounts for more than 10% of in-hospital mortality. The risk for developing infections and sepsis is high in patients with type 2 diabetes mellitus. Also, the prognosis of infection can be worsened by the presence of type 2 diabetes mellitus. This leads to an increased rate of mortality and morbidity in type 2 diabetes mellitus patients with sepsis[2].

Sepsis that is complicated by acute organ dysfunction accounts for around half of intensive care unit resource utilization[3,4]. Its associated morbidity and mortality are higher when compared to sepsis without acute organ dysfunction. The mortality rate caused due to severe sepsis varies

from 28.6% to 49.6%[3,5]. Advanced age, chronic alcoholism, and an immunosuppressed state are the various factors that can negatively impact the treatment outcome of severe sepsis[6].

Different types of organisms can cause sepsis. The most common organism isolated in septic patients is the gram-negative bacteria. Recently, the proportion of patients with severe infections due to gram-positive bacteria has increased. It accounts for half of the incidents of septicemia and severe systemic infections.

The hospital mortality rate identified in the bacteremic diabetic patients and non-diabetic patients is 24.1% and 44.0%. Diabetic patients with bacteremia are less likely to develop septic shock and acute renal failure with 4% and 7% risk as compared to non-diabetic patients with 13% and 19% risk, respectively. The mortality rate for diabetic patients and non-diabetic patients with bacteremia is identified to be 21.6% and 37.2%.

The appropriate selection of empirical antibiotics based on the pattern of local antibiotic resistance can reduce the mortality rate and increase the rational use of antibiotics. Pradipta et al[7] conducted a retrospective observational study in which levofloxacin, ceftazidime, ciprofloxacin, cefotaxime, ceftriaxone, and erythromycin were the most frequently used antibiotics in patients with sepsis with an average resistance of above 50%. In a cross-sectional study conducted by Anvarinejad et al[8], multidrug resistance was identified in 91% of the isolates and methicillin resistance in 78% of *S. aureus* isolates. Whereas 53% of the gram-negative species were identified as positive for extended-spectrum *β-lactamase*.

The mortality ascribed to sepsis is decreasing because of improvements in treatment and nursing, but still, sepsis remains a critical problem, especially in diabetic patients. The influence of diabetes mellitus on the outcomes of sepsis remains controversial. The antimicrobial resistance of bacterial pathogens in the diabetic population with infection is less investigated. Routine bacteriological profiling along with their antibiotic resistance patterns should be considered as a necessary component in the management of sepsis. A knowledge of these patterns is essential when local policies on the use of antibiotics are being devised. The present study was conducted to compare the bacterial diversity in sepsis patients under ICU care and their antibiotic resistance pattern in diabetic patients and nondiabetic patients.

PATIENTS AND METHODS

The prospective study included bacterial isolates identified from various samples collected at In-patient department (IPD) of Max Super Specialty Hospital, Vaishali, a tertiary care facility of Delhi-NCR between March 2018 to March 2019.

The study was approved by the Ethical Committee of Max Super Specialty Hospital, Vaishali, Ghaziabad, India.

Bacterial Identification Method and Antibiotic Susceptibility Testing

Bacterial isolates were recovered from different clinical samples including blood, urine, respiratory secretions and others. The isolates were identified by standard microbiological methods and the automated Vitek 2 system. All repeat isolates and the isolate recovered from the regions of most likely colonization such as throat swab, perianal swab etc. were excluded from the study. Six major classes of antibiotics, namely, beta lactams, fluoroquinolones, carbapenems, macrolides, aminoglycosides, and sulfamethoxazole-trimethoprim, in addition to colistin and tigecycline, were used to determine the antibiotic susceptibility pattern of isolates.

Statistical Analysis

Statistical analysis was performed by the SPSS program for Windows, version 17.0 (SPSS, Chicago, IL, USA). Continuous variables are presented as mean ± SD, and categorical variables are presented as absolute numbers and percentage. Data were checked for normality before statistical analysis. Normally distributed continuous variables were compared using the unpaired *t*-test, whereas the Mann-Whitney U test was used for those variables that were not normally distributed. Categorical variables were analyzed using either the Chi-square test or Fisher's exact test. $p<0.05$ was considered statistically significant.

RESULTS

A total of 495 participants were included in the final analysis, with 240 participants in the diabetic group and 255 participants in the non-diabetic group. The mean age of participants in the diabetic group was 65.43 ± 10.36 and 60.75 ± 15.15 in the non-diabetic group. The difference in mean age between the study group was statistically significant (p-value<0.05). Out of 240 diabetic patients, 133 (55.42%) were male, and 107 (44.58%) were female. Out of 255 non-diabetic patients, 171 (67.06%) were male, and 84 (32.94%) were female. Lower respiratory tract infection (LRTI) was observed to be 101 (42.26%) in diabetic patients, whereas in non-diabetic patients, it was 133 (52.16%). Other sources of sepsis were Blood stream infection (BSI) which was 58 (24.27%) in diabetic and 55 (21.57%) in non-diabetic patients, urinary tract

Table 1. Comparison of culture report between study group (N=470).

Culture Report	Diabetes Mellitus	
	Yes (N=224)	No (N=246)
Acinetobacter	22 (9.82%)	29 (11.79%)
Enterococcus	19 (8.48%)	13 (5.28%)
Escherichia Coli	52 (23.21%)	42 (17.07%)
Klebsiella	70 (31.25%)	82 (33.33%)
Others	21 (9.38%)	18 (7.32%)
Pseudomonas	15 (6.7%)	32 (13.01%)
Staphylococcus	25 (11.16%)	30 (12.2%)

infection (UTI) in diabetic and non-diabetic patients were 57 (23.85%) and 47 (18.43%), respectively along with skin and subcutaneous tissue infection (SSTI) were 23 (9.62%) and 20 (7.84%) in diabetic and non-diabetic patients, respectively. The most common isolated organism was *Klebsiella* in both diabetic {70, (31.25%)} and non-diabetic patients {82, (33.33%)}, respectively. Other organisms isolated were *Escherichia coli* {52(23.21%) in diabetic and 42(17.07%) in non-diabetic}, *Staphylococcus* {25(11.16%) in diabetic, 30(12.2%) in non-diabetic}, *Acinetobacter* {22(9.82%) in diabetic, 29(11.79%) in non-diabetic), *Enterococcus* {19(8.48%) in diabetic, 13(5.28%) in non-diabetic}and other organisms (*Citrobacter, Providencia, Morgenella, Stenotrophomonas, Proteus, Myroides, Elizabethkingia*) {21(9.38%) in diabetic and 18 (7.32%) non-diabetic} (Table 1).

Out of total isolates, culture revealed growth of *Candida* in 16(6.67%) diabetic patients and 9(3.53%) non-diabetic patients. Diabetic patients have *Candida albicans* {10(62.5%)}, and non-diabetic patients have growth of *Candida tropicalis* {6(66.67%)}.

Among 223 diabetic patients, Acinetobacter was primarily isolated in patients with LRTI {15(68.18%} whereas prevalence in BSI, SSTI, UTI was 4 (18.18%), 2 (9.09%), 1 (4.55%), respectively. A major source of *Enterococcus* was patients with UTI {10(52.63%)}, whereas prevalence in BSI, LRTI, SSTI was 5 (26.32%), 3 (15.79%), 1 (5.26%), respectively. *Escherichia coli* was isolated in 22 (43.14%) patients with UTI; the rest of the other sources revealed 11 (21.57%) from LRTI, 9 (17.65%) from BSI, 9 (17.65%) from SSTI. *Klebsiella* was isolated in 43 (61.43%) LRTI patients; the rest of the other sources revealed 12 (17.14%) in UTI, 12 (17.14%) in BSI, 3 (4.29%) in SSTI. A major source of *Pseudomonas* was LRTI {7(46.67%), other sources revealed 4 (26.67%) in SSTI, 2(13.33%) in BSI, 2 (13.33%) in UTI. *Staphylococcus* was isolated in patients with BSI {17(68%)}, rest other sources were UTI {4(16%)}, LRTI {3(12%)}, SSTI {1(4%)}, respectively. For others, the major source was LRTI for 13 (61.9%) patients. The difference in culture reports between the source was statistically significant (p-value<0.05) (Table 2).

Among the non-diabetic patients, the major source of *Acinetobacter* was LRTI patients 19 (65.52%), the rest of other source revealed 8 (27.59%) in BSI, 2 (6.9%) in SSTI patients. *Enterococcus* was isolated in BSI and UTI patients 4 (30.77%) respectively, while 2 (15.38%) was isolated in SSTI patients. For *Escherichia Coli*, the major source was UTI patients 17 (40.48%), and prevalence in other sources were LRTI patients 13 (30.95%), BSI patients 8 (19.05%), SSTI patients 4 (9.52%). For *Klebsiella*, the major source was LRTI for 54 (65.85%) patients, and the rest of the other sources revealed BSI patients 12 (14.63%), UTI patients 10 (12.2%), and SSTI patients 6 (7.32%). For *Pseudomonas*, the major source was LRTI patients for 19 (59.38%), the rest of the other sources revealed UTI, BSI, SSTI patients 7 (21.88%), 3 (9.38%), 3 (9.38%). For *Staphylococcus*, the major source was BSI for 16 (53.33%) patients and LRTI for 11 (36.67%) patients. For others, the major source was LRTI for 9 (50%) participants (Table 3).

Antibiotic Resistance Pattern

Among the study population with culture report as *Acinetobacter*, there was not a statistically significant difference in drugs like Amikacin, Gentamicin, Colistin, Cefepime, Ceftriaxone, Ciprofloxacin, Imipenem, Meropenem, and Piperacillin/Tazobactum, Cefoperazone/Sulbactum between the study group (p-value>0.05) while for Trimethoprim-sulfamethoxazole there was a statistically significant difference between study group (p-value<0.05) (***Supplementary Table 1***).

Table 2. Comparison of culture report across source in diabetic patients (N=223).

Culture Report	Source				Chi square	*p*-value
	BSI	LRTI	SSTI	UTI		
Acinetobacter (N=22)	4 (18.18%)	15 (68.18%)	2 (9.09%)	1 (4.55%)		
Enterococcus (N=19)	5 (26.32%)	3 (15.79%)	1 (5.26%)	10 (52.63%)		
Escherichia Coli (N=51)	9 (17.65%)	11 (21.57%)	9 (17.65%)	22 (43.14%)		
Klebsiella (N=70)	12 (17.14%)	43 (61.43%)	3 (4.29%)	12 (17.14%)	82.463	<0.001
Others (N=21)	4 (19.05%)	13 (61.9%)	2 (9.52%)	2 (9.52%)		
Pseudomonas (N=15)	2 (13.33%)	7 (46.67%)	4 (26.67%)	2 (13.33%)		
Staphylococcus (N=25)	17 (68%)	3 (12%)	1 (4%)	4 (16%)		

Table 3. Comparison of culture across source in non-diabetic patients (N=246).

Culture Report	Source			
	BSI	LRTI	SSTI	UTI
Acinetobacter (N=29)	8 (27.59%)	19 (65.52%)	2 (6.9%)	0 (0%)
Enterococcus (N=13)	4 (30.77%)	3 (23.08%)	2 (15.38%)	4 (30.77%)
Escherichia Coli (N=42)	8 (19.05%)	13 (30.95%)	4 (9.52%)	17 (40.48%)
Klebsiella (N=82)	12 (14.63%)	54 (65.85%)	6 (7.32%)	10 (12.2%)
Others (N=18)	2 (11.11%)	9 (50%)	3 (16.67%)	4 (22.22%)
Pseudomonas (N=32)	3 (9.38%)	19 (59.38%)	3 (9.38%)	7 (21.88%)
Staphylococcus (N=30)	16 (53.33%)	11 (36.67%)	0 (0%)	3 (10%)

Among the study population with culture report as *E. Coli*, there was not a statistically significant difference in drugs belonging to Nitrofurantoin, Cefepime, Cefuroxime, Ceftriaxone, Ciprofloxacin, Imipenem, Ertapenem, Meropenem, Amoxicillin, Ampicillin, and Piperacillin/Tazobactum, Cefoperazone/Sulbactum, Amoxicillin/Clavulanic acid between the study group (p-value >0.05) while for Trimethoprim-sulfamethoxazole there was a statistically significant difference between study group (p-value <0.05) (***Supplementary Table 2***). Among the study population with culture report as *Klebsiella*, there was not a statistically significant difference in the following drugs, Nitrofurantoin, Cefuroxime, Ceftriaxone, Amoxicillin, Ampicillin, and Tigecycline between the study group (p-value >0.05) while for Imipenem, Ertapenem, Meropenem, Cefoperazone/Sulbactum, Piperacillin/Tazobactum, Amoxicillin/Clavulanic acid and Cefepime, there was a statistically significant difference between study group (p-value <0.05) (***Supplementary Table 3***). Among the study population with culture report as *Staphylococcus*, there was not a statistically significant difference in any of the drugs belonging to Oxacillin, Ampicillin, Benzylpenicillin, Clindamycin, Gentamicin, Linezolid, Teicoplanin, Vancomycin, Nitrofurantoin, Cefoxitin, Ciprofloxacin, Levofloxacin, and Erythromycin between the study group (p-value>0.05) (***Supplementary Table 4***). Among the study population with culture report as *Pseudomonas*, there was not a statistically significant difference in drugs belonging to Ceftazidime, Cefepime, Piperacillin/Tazobactum, Ticarcillin/Clavulanic acid, Cefoperazone/Sulbactum, Netilmicin, Amikacin, Gentamicin, Tobramicin, Benzylpenicillin, Lincomycin, Nitrofurantoin, Ciprofloxacin, Levofloxacin, Imipenem, Meropenem, Doripenem between the study group (p-value>0.05) (***Supplementary Table 5***). Among the study population with culture report as *Enterococcus*, there was not a statistically significant difference in drugs belonging to Linezolid, Gentamicin, Nitrofurantoin and Tetracycline between the diabetes mellitus (p-value>0.05), while for Teicoplanin, Vancomycin there was a statistically significant difference between the study group (p-value<0.05) (***Supplementary Table 6***).

Out of 240 participants in the diabetic group, 110 (46.03%) participants had outcomes as death, and 130 (53.97%) participants had outcomes as discharged. Out of 255 participants in the non-diabetic group, 103 (40.39%) participants had the outcome as death, and 152 (59.38%) participants had the outcome as discharged. The difference in outcome between the study group was not statistically significant (p-value>0.05).

DISCUSSION

The risk of developing infections and sepsis is high in patients with type 2 diabetes mellitus. Also, the prognosis of infection can be worsened by the presence of type 2 diabetes mellitus. It leads to an increased rate of mortality and morbidity in type 2 diabetes mellitus patients with sepsis[2]. Antimicrobial stewardship is defined as the optimal selection, dosage, and duration of antimicrobial treatment that can result in the best clinical outcome for the management or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance. Work with health care practitioners in order to help each patient receive the most appropriate antimicrobial with the correct dose and duration, prevention of antimicrobial overuse, misuse, and abuse, and minimizing the development of resistance are the goals associated with antimicrobial stewardship[9]. Antimicrobial resistance of bacterial pathogens in the diabetic population with infection is less investigated. Routine bacteriological profiling along with their antibiotic resistance patterns should be considered as a necessary component in the management of sepsis. A knowledge of these patterns is essential when local policies on the use of antibiotics are being devised. The present study was conducted to compare the bacteriological diversity in patients with sepsis under ICU care and compare their antibiotic resistance pattern in diabetic patients and non-diabetic patients.

A total of 495 participants were included in the final analysis, with 240 participants in the diabetic group and 255 participants in the non-diabetic group.

In the present study, the mean age of participants in the diabetic group was higher as compared to the non-diabetic group. Similarly, in the retrospective study of Trivedi et al[10], in 115 participants, the mean age of the participants was greater in the diabetic group as compared to the non-diabetic group. The present study was conducted in a tertiary care hospital that caters both urban and rural population and have huge burden of critical referral cases with aging population.

In the current study, the majority of the participants were males in the diabetic and non-diabetic groups. In Trivedi et al[10], the majority of the participants were females in the diabetic group, whereas, in the non-diabetic group majority were males. The diabetic group showed contradictory results, whereas the non-diabetic group showed resembles our study results.

In the present study, the source was identified as LRTI in the majority of cases, followed by BSI, UTI, and SSTI in both the diabetic and non-diabetic groups. In a prospective cohort study performed by Muller et al[11], in which URTI was identified as the major source followed by UTI, MSMI, LRTI in the diabetic and non-diabetic group, which is contradictory to our study results. In the study of Esper et al[12], the source of infection of most participants was found in the respiratory tract in both the diabetic and non-diabetic population followed by genitourinary, gastrointestinal, skin and soft tissue and bone.

In the diabetic population, the Culture Report showed *Acinetobacter, Enterococcus, Escherichia Coli, Klebsiella, Staphylococcus*, and *Pseudomonas* species whereas, in non-diabetic patients, *Acinetobacter, Enterococcus, Escherichia Coli, Klebsiella, Staphylococcus*, and *Pseudomonas* species were identified in the culture report. Acharya et al[13] conducted a prospective cross-sectional study in 180 patients in which *Escherichia coli*, *Klebsiella* sps, *Enterococcus* sps, *Enterobacter* sps, *Citrobacter* sps, *Proteus* sps, were identified in diabetic patients and non-diabetic patients. In a population of 200 participants Akhand et al[14] performed a study in which the culture report showed *Escherichia coli* 64.5% and 66.7%, *Klebsiella* 22.6% and 12.5%, *Enterococcus* 6.5% and 4.2%, *Enterobacter* 0% and 4.2%, *Citrobacter* 3.2% and 0% and *Proteus* 0% and 8.4% in diabetic and non-diabetic population respectively.

Among the diabetic people, BSI and UTI were identified as the major source for *Enterococcus* and *Staphylococcus*. Whereas the major source was LRTI and UTI for *Escherichia Coli* and *Klebsiella*. For *Pseudomonas*, the major source was LRTI and SSTI, while BSI and LRTI were the source of infection in Acinetobacter growing isolates.

Among the non -diabetic people, BSI, LRTI, and UTI were identified as the major source for *Acinetobacter, Enterococcus, Escherichia Coli, Klebsiella, Staphylococcus*, and *Pseudomonas* species, respectively.

In the present study, the *Acinetobacter* was most sensitive to colistin, Trimethoprim-sulfamethoxazole, and tigecycline whereas, resistant to cefepime, ceftriaxone, ciprofloxacin in diabetic patients. Similarly, in non-diabetic patients, *Acinetobacter* was most sensitive to colistin and tigecycline and resistant to cefepime, ciprofloxacin, imipenem. Ahmadishooli et al[15] conducted a study in 84 diabetic patients in which the *Acinetobacter* was sensitive to ampicillin-sulbactam, cefepime, ceftriaxone, gentamycin, ciprofloxacin, cotrimoxazole, amikacin, meropenem, imipenem, ceftazidime, and piperacillin/tazobactam, whereas resistant to amikacin.

In the current study, the *Escherichia coli* was sensitive to tigecycline, colistin, and amikacin while it was resistant to amoxicillin, ampicillin, and ciprofloxacin in diabetic patients. Similarly, in non-diabetic patients, *Escherichia coli* was sensitive to tigecycline, colistin, and amikacin and resistant to amoxicillin, ampicillin, and ciprofloxacin. In Thapa et al[16], *Escherichia coli* isolates were sensitive to Amikacin, Nitrofurantoin, Cotrimoxazole and resistant to Nalidixic acid, Norfloxacin, Ciprofloxacin in diabetic patients. Whereas, in non-diabetics, all *Escherichia coli* isolates were sensitive to Cotrimoxazole, Amikacin, Nitrofurantoin and resistant to Nalidixic acid, Norfloxacin, and Cotrimoxazole.

In the current study, *Klebsiella* was most sensitive to colistin and tigecycline and resistant to amoxicillin, ceftriaxone, and cefuroxime in diabetic patients. Whereas, in non-diabetic patients, *Klebsiella* was most sensitive to colistin and tigecycline and resistant to amoxicillin, ceftriaxone, and cefuroxime. In Thapa et al[16], all the *Klebsiella* isolates were sensitive to almost all antibiotics and did not show any resistant pattern in diabetic patients; in non-diabetic patients, all isolates were sensitive to cotrimoxazole, amikacin, nitrofurantoin and resistant to nalidixic acid.

In the present study, the *Staphylococcus* was most sensitive to daptomycin, teicoplanin, vancomycin and resistant to ampicillin and benzyl penicillin in diabetic patients whereas, in non-diabetic patients, *Staphylococcus* was most sensitive to daptomycin, teicoplanin, vancomycin and resistant to ampicillin and benzyl penicillin. Thapa et al[16] performed an e cross-sectional descriptive study in 601 subjects in which the *Staphylococcus aureus* isolates were sensitive to gentamicin, cefotaxime, cotrimoxazole, and ciprofloxacin and resistant to amikacin, oxacillin, and azithromycin in diabetic patients whereas, in non-diabetic all isolates were sensitive to azithromycin, gentamicin, cefotaxime, cotrimoxazole, vancomycin and levofloxacin and resistant to oxacillin which was contradictory to our study results.

In the present study, *Pseudomonas* was most sensitive to amikacin, imipenem, meropenem and resistant to ticarcillin/clavulanic acid, netilmicin, and tobramycin in diabetic patients whereas, in non-diabetic patients, the *Pseudomonas* was sensitive to amikacin, imipenem, and doripenem and resistant to ticarcillin/clavulanic acid, netilmicin and tobramycin. In Jain et al[17], the *Pseudomonas* culture isolates were sensitive to amikacin, imipenem, meropenem, piperacillin-tazobactam combination, tigecycline, ciprofloxacin, and levofloxacin in diabetic patients.

In the present study, *Enterococcus* was most sensitive to tigecycline, linezolid and resistant to ciprofloxacin and levofloxacin in diabetic patients. Whereas, in non-diabetic patients, *Enterococcus* was most sensitive to tigecycline, linezolid, and resistant to ciprofloxacin and levofloxacin in diabetic patients. Jain et al[17] performed a study in 185 subjects in which *Enterococcus* culture isolates were sensitive to linezolid, daptomycin, teicoplanin, tigecycline, benzylpenicillin, vancomycin, ciprofloxacin, levofloxacin, erythromycin, and tetracycline in diabetic patients.

In the present study, the mortality rate was identified as high in the diabetic group as compared to the non-di-

Table 4. Comparison of outcome between study group (N=494).

Outcome	Diabetes Mellitus		Chi square	*p*-value
	Yes (N=240)	No (N=255)		
Death	110 (46.03%)	103 (40.39%)	1.469	0.226
Discharge	130 (53.97%)	152 (59.38%)		

abetic group. Whereas the discharge rate was high in the non-diabetic patients as compared to diabetic patients. Similarly, in the Moutzouri et al[18], the mortality in diabetic septic patients was higher as compared to the mortality in the non-diabetic population (Table 4).

CONCLUSIONS

Antimicrobial resistance has been increasing at an alarming rate worldwide. One of the few major factors that lead to an increase in resistance is the indiscriminate, injudicious use and underdosing of antibiotics. Uncontrolled blood sugar in the sea of an existing pandemic of diabetes mellitus adds to the increasing resistance, leading to high mortality.

The isolates in the present study revealed *Klebsiella* to be the most prevalent organism in both diabetic and non-diabetic patients, whereas the lowest prevalence in diabetic patients was that of *Pseudomonas*. *Enterococcus* was the lowest in prevalence among non-diabetic patients. Colistin was found to be highly sensitive in *Klebsiella, Acinetobacter,* and *Escherichia coli* in both diabetic and non-diabetic patients. *Acinetobacter* showed high resistance to cephalosporin, fluoroquinolones, carbapenems in both diabetic and non-diabetic patients; however, sensitivity was lower for tigecycline in diabetic patients when compared to non-diabetic patients.

Escherichia coli was highly resistant to beta-lactam, beta-lactam/beta-lactamase inhibitor, cephalosporins, fluoroquinolones in both diabetic and non-diabetic patients, whereas tigecycline sensitivity was much lower in diabetic when compared to non-diabetic. Isolates showing the growth of *Klebsiella* revealed significant resistance to cefepime, beta-lactam, beta-lactam/beta-lactamase inhibitor, carbapenems, aminoglycosides, nitrofurantoin among diabetics in comparison to non-diabetic patients. *Pseudomonas* was highly sensitive to polymyxin B in both groups, whereas diabetic patients showed increased resistance to carbapenems, beta-lactam/beta-lactamase inhibitor, aminoglycosides, cephalosporins, and fluoroquinolones. *Enterococcus* and *Staphylococcus* were gram-positive bacteria that were seen in a significant number of isolates. *Enterococcus* showed high resistance to beta-lactams, aminoglycosides, fluoroquinolones, and macrolides in both diabetic and non-diabetic patients. However, in the group of diabetic patients, there was a significant increase in resistance to linezolid, glycopeptides, nitrofurantoin, and tetracycline, when compared with non-diabetics. Tigecycline showed resistance in half isolates among both diabetic and non-diabetic patients. Another gram-positive bacterium, *Staphylococcus*, revealed high resistance to beta-lactams, linezolid, fluoroquinolones, macrolides in both groups. This study conducted in a tertiary care hospital will help in understanding the diversity of bacteria prevalent in our community, which would help in formulating a better empirical antibiotic usage policy with proper implementation of antibiotic stewardship. Empirical antibiotic therapy should be prescribed only after taking sample for performing antimicrobial susceptibility testing and targeted therapy is to be done according to the results of the culture and susceptibility testing, in order to obtain a better outcome.

Conflict of Interest:
The authors declare that they have no conflict of interests.

Ethics Approval:
Approval issued by Ethical Committee of Max Super Specialty Hospital, Vaishali, Ghaziabad, India.

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All data are available upon reasonable request by contacting the Corresponding Author of the manuscript.

Authors Contributions:
The authors confirm contribution to the paper as follows: research conception and design: SP, PNC, NPS; data acquisition: SP, GG; analysis or interpretation of results: SP, AKG, VP; draft manuscript preparation and revision: SP, GG, AKG, PNC, VP, NPS. All authors reviewed the results and approved the final version of the manuscript.

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