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Bacterial Bloodstream Infections – Prevalence, Etiology, and their Antibiotic Susceptibility Profile in Mumbai City

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aim: To study bacterial bloodstream infections concerning prevalence, etiology, and antibiotic susceptibility profile of pathogens in Mumbai City
Study Design: Retrospective study
Place and Duration of Study: Department of Microbiology, InfeXn Laboratories Pvt. Ltd., Thane One-year duration: January 2019- December 2019
Methodology: The present retrospective study was performed on around 9397 adult and pediatric blood samples by using a rapid, accurate, and high throughput automated blood culture system for timely diagnosis of BSI.
Results and Discussion: Bloodstream infection (BSIs) is considered a medical emergency as it is associated with high morbidity and mortality worldwide. The prevalence of BSI-causing bacteria and their Antibiotic susceptibility (AST) profile vary as per age, season, geographical location, etc. With a large cohort of 9397 samples, the total positivity rate was 17.47 % with gram-negative bacteria (67.69%) being more common than gram-positive (32.30%) in both adult and pediatric populations, with a peak in the Monsoon season. *Escherichia coli (26.17%) and Klebsiella pneumoniae* (27.31%) were the most isolated pathogens in the adult and pediatric populations, respectively. Carbapenemase production was seen highest in the non-fermentor group of bacteria *(42.85%)* whereas ESBL production was seen more in the Enterobacterals group (53%). Except for MRSA, gram-positive bacteria showed a very good susceptibility profile to the listed antibiotics. There was no case of VRE observed in the study.

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Conclusion: The study highlights the need for regular monitoring of BSI-causing bacteria and their antibiogram, which can help better to formulate empirical treatment strategies, controlled use of antibiotics, monitoring trends in drug resistance, and antibiotic stewardship.

Keywords: Bloodstream Infections (BSI); sepsis; automated blood cultures; ESBL and carbapenemase producers; antimicrobial resistance.

1. INTRODUCTION

BSIs are caused by a wide range of bacteria (bacteremia) and fungi (fungemia) in the blood. The sepsis syndrome ranges from SIRS (Systemic Inflammatory Response Syndrome) to septic shocks and eventually death. Hence, accurate and early diagnosis of BSI-causing organisms and their antibiotic susceptibility profile is a crucial step in patient management.

Conventionally, Blood culture is considered a gold standard method for the identification of organisms and antibiotic sensitivity testing. Molecular methods like PCR or sequencing provide a faster diagnosis with more sensitivity compared to blood culture however these tests require a dedicated setup, expert handling, and higher maintenance cost making them not so preferred option in economically restrained areas. Also, it is not possible to obtain an antibiotic profile with MIC values using these techniques. Thus, blood cultures cannot be replaced totally, rather are upgraded with automation with the advent of automated blood culture monitoring systems.

The etiological profile of BSI varies with geographical regions [1,2-4]. Regular surveillance of a particular region regarding the same is necessary to ensure proper treatment strategy. Many such prospective and retrospective studies related to immune-compromised, cancer, and pediatric patients are carried out in India and globally [1,5,6,2,3,4,7-22]. The present retrospective study gives blood culture analysis of a total of 9397 patients tested in one year in a diagnostic laboratory, Mumbai for the presence of aerobic bacteria in the blood. The microbiological profile and antibiotic sensitivity profile were analyzed with the help of automated identification systems.

2. MATERIALS AND METHODS

The retrospective study was conducted for one year in a private infectious disease testing laboratory in Mumbai. Blood samples were collected from primary, secondary, and tertiary care hospitals across the city. The standard Month wise positivity was as follows:

guidelines for sample collection and transportation were followed. 8-10ml of blood from adult patients and 1-3 ml from pediatric patients were collected in respective BD BACTEC^{TM} plus Aerobic culture bottles. Properly labeled, aseptically transferred, leak-proof, room temperature maintained, timely transported blood samples were included in the study. The blood culture bottles were loaded in the BD BACTEC FX^{TM} instrument immediately upon receiving them in the central processing laboratory.

Every culture bottle was observed for five days for positivity. At any point during incubation, the instrument flags a positive blood culture, it was subcultured on Sheep Blood agar and MacConkey's agar plate. After 24hrs. of incubation at 37°C, well-isolated colonies with similar morphology were processed. The Gram nature and colony morphology were taken into account for the selection of appropriate ID and AST panels. The density of the inoculum was checked with the help of a BD Nephelometer and adjusted to 0.5 McFarland. The inoculated broths were tested for ID and AST with BD Phoenix 100^{TM} instrument as per the standard protocol.

The data of a total of 9397 blood samples from 1st January 2019 to 31st December 2019 were taken into account for retrospective analysis. The analysis was carried out regarding positivity, patients' demographics, bacterial identification profile, and antibiotic susceptibility profile. AST analysis was carried out as per the standard CLSI guidelines [23]. Quality control was performed for the tests using known bacterial ATCC strains as per protocol.

3. RESULTS

3.1 Positivity of Bloodstream Bacterial Infections

Out of 9397 blood samples, 4902 were adults, and 4495 were pediatric patients. Of these, 1647/ 9397 (17.52%) tested positive. These include 736 (15.01%) adult positives and 911(20.25%) pediatric.

Table 1. Month wise positive blood samples for the year 2019

Paed	Month	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Total
	Positive	62	51	68	54	65	78	88	84	59	44	41	42	911
Adult	**Month**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sept**	**Oct**	**Nov**	**Dec**	**Total**
	Positive	71	60	81	62	72	99	102	113	78	61	56	56	736

3.2 Bacterial Profile of Positive Cultures

Table 2. Bacterial profile of positive blood samples

Bacteria		Adult positives	Total N=736	Paed. Positives	Total N=911	
Gram Negative isolates	*Escherichia coli*	128	**489**	145	**626**	Total Gram Negative Isolates =1115
	Klebsiella pneumonia	96		171		
	Salmonella typhi	65		122		
	Acinetobacter baumanni	82		68		
	Pseudomonas aeruginosa	97		109		
	Proteus mirabilis	21		11		
Gram-Positive isolates	*Staphylococcus aureus*	34	**247**	78	**285**	Total Gram-Positive isolates =532
	Enterococcus faecalis	57		28		
	MRSA(Methicillin-Resistant *Staphylococcus aureus*)	77		21		
	Streptococcus pyogenes	38		46		
	Streptococcus pneumoniae	41		78		
	CONS(Coagulase-negative *Staphylococcus aureus*	-		34		

3.3 Antibiotic Susceptibility Patterns of Isolates

The figures show % of susceptible bacteria against antibiotics.

3.3.1 Antibiotic susceptibility patterns of gram-negative bacterial isolates

Antibiotic Susceptibility of isolated pathogens was interpreted and reported as per CLSI guidelines 2019. Accordingly, susceptibility profiles for Enterobacterals (*E. coli, K. pneumonia, P. mirabilis),* are described together. Similarly, susceptibility non-lactose fermenters like *P. aeruginosa* and *A. baumanii* are described together. The bacteria exhibit intrinsic resistance to some antibiotics, hence they are excluded from the respective calculations.

3.3.1.1 Antibiotic susceptibility patterns of gram-negative lactose fermenters (LF) bacterial isolates - enterobacterals

Enterobacterals showed 7-37% sensitivity for β-lactam antibiotics (penicillin derivatives, cephalosporins), 45% sensitivity for cyclin group antibiotics, 68-73% sensitivity for penem group antibiotics, and 97% sensitivity for Colistin. *S. typhi* showed 100% sensitivity for the antibiotics-Ampicillin, Ceftriaxone, Cotrimoxazole, Ciprofloxacin, and Chloramphenicol.

3.3.1.2 Antibiotic Susceptibility patterns of gram-negative non-lactose fermenter (NLF) bacterial isolates- Pseudomonas aeruginosa and Acinetobacter baumanni

Out of the listed β- lactam antibiotics, *Pseudomonas aeruginosa* and *Acinetobacter baumanni* showed 22.5-36.8% sensitivity for Ceftazidime and Cefepime drugs. Cyclin drugs were effective against *A. baumanni* with 28.7% sensitivity. Both the pathogens showed 55.9-58.4% sensitivity for penem drugs and 90.7% sensitivity for Colistin.

3.3.3 Antibiotic Susceptibility patterns of Gram-positive bacterial isolates

3.3.3.1 Staphylococcus aureus and MRSA

S. aureus showed 100% sensitivity for listed β lactam, penem groups, glycopeptides (Vancomycin, Clindamycin, etc.) of antibiotics, 60% for cyclin group of antibiotics. MRSA was observed for 100% resistance to the above-mentioned antibiotics except for glycopeptides groups.

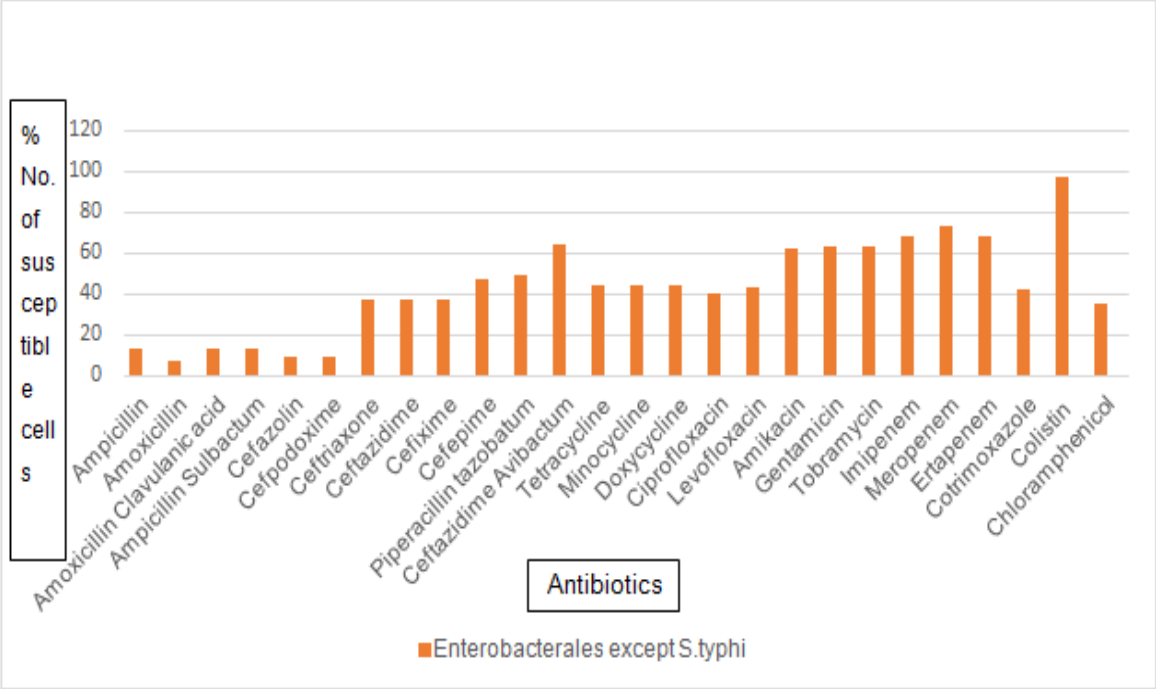

Fig. 1. Antibiotic Susceptibility patterns of Gram Negative bacterial isolates- Enterobacterals except *Salmonella typhi*

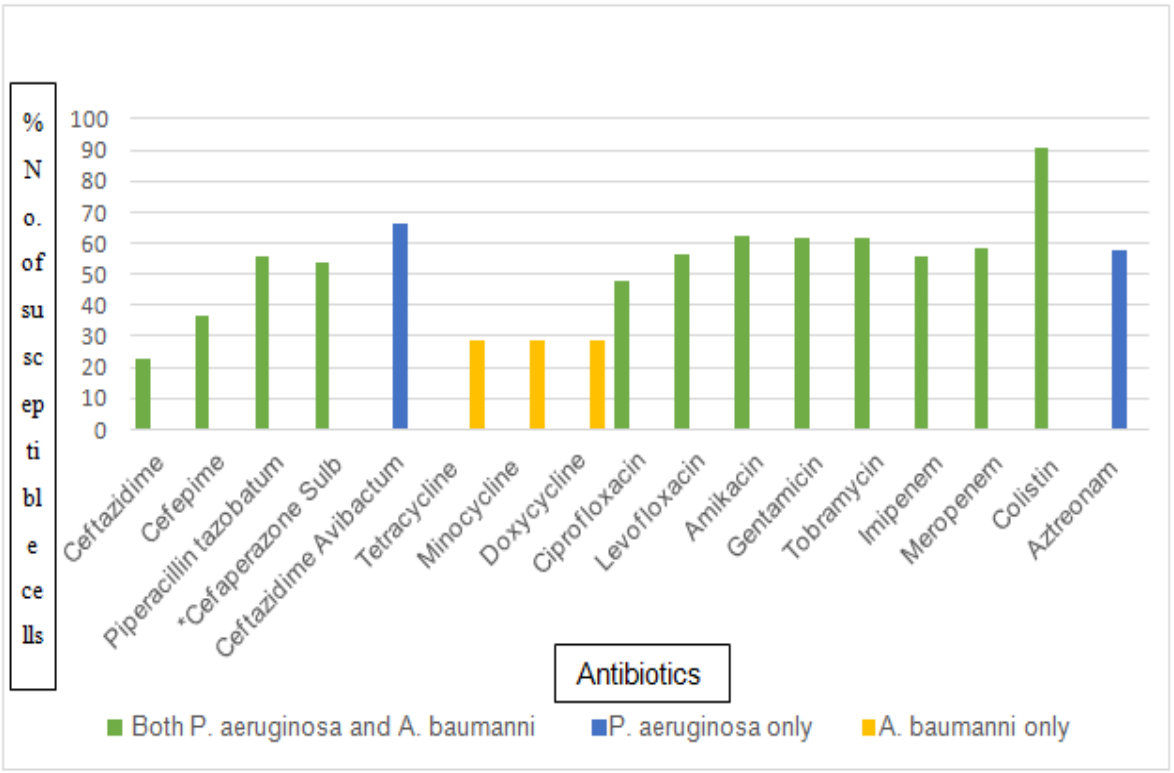

Fig. 2. Antibiotic Susceptibility patterns of Gram Negative bacterial isolates- *Pseudomonas aeruginosa* and *Acinetobacter baumanni*

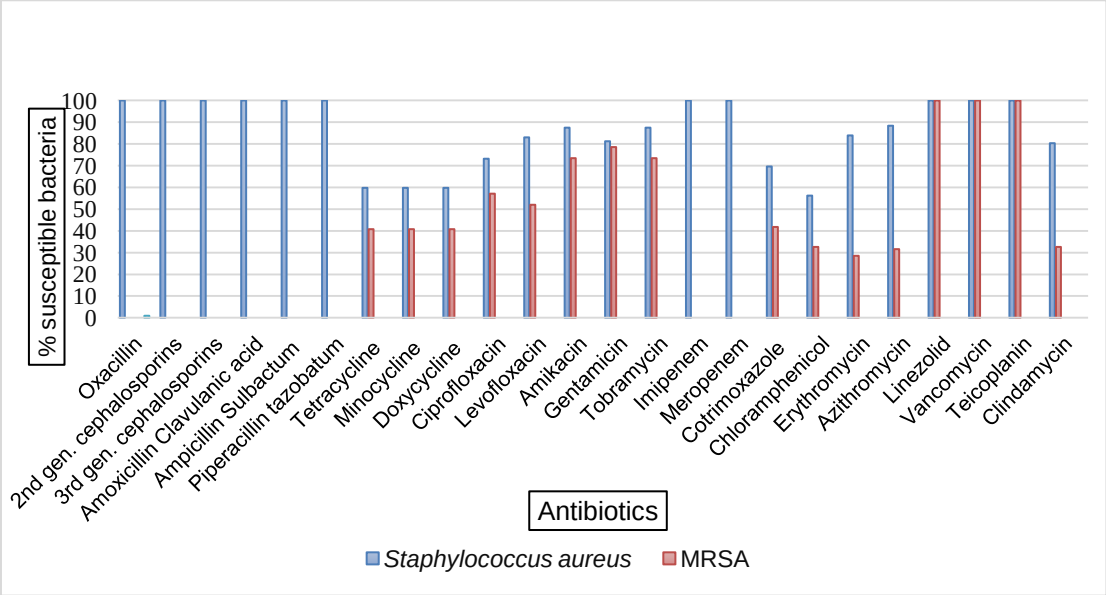

Fig. 3. Antibiotic Susceptibility patterns of Gram-Positive bacterial isolates: S. aureus and & MRSA

3.3.3.2 Antibiotic susceptibility patterns of other gram-positive bacterial isolates

E. faecalis showed 100% sensitivity to Daptomycin, Linezolid, Teicoplanin, Vancomycin, and Doxycycline and 24-35% sensitivity to other antibiotics. *S. pyogenes* showed 100% sensitivity for Ampicillin, Cefepime, Ertapenem, Vancomycin, Daptomycin, Erythromycin, Meropenem, Tetracyclin, Levofloxacin, Chloramphenicol, Clindamycin, Linezolid. *S. pneumoniae* showed 100% sensitivity for Amoxicillin, Amoxicillin-Clavulanic acid, Cefepime, Cefotaxime, Ceftriaxone, Cefuroxime, Meropenem, Imipenem, Ertapenem, Vancomycin, Erythromycin, Tetracycline, Doxycycline, Levofloxacin, Co-trimoxazole, Clindamycin, Linezolid.

3.4 ESBL and Carbapanemase Producers

Out of the Gram-negative bacteria, 30.34% of Enterobacterales, and 42.85% of Nonfermenters were carbapenemase producers. 53% of Enterobacterales and 41% of Nonfermenters were ESBL producers.

4. DISCUSSION

Sepsis or septicemia is a medical emergency when any infection of the body enters the bloodstream and triggers the cascading inflammatory response even resulting in death if not treated properly. Hence, timely detection of BSI is important to ensure proper treatment strategies.

The present study shows a 17.52% presence of pathogens in the bloodstream which is consistent with similar studies like Dash M. et al. [4] Prashant Meshram et al. [14] Some studies show a lesser percentage (7.5-10%) positivity of BSI like Tsering Yangzom et.al. [21], Laxmi Kant Khanal et al. [12], J.P Sonawane et al. [9], and a higher percentage (27-47%) like Radha Rani et al. [15], D. Saranya et al [3] The variations may be due to different patient populations, disease prevention and control policies, blood culture systems, and geographical locations. The pediatric population exhibits a higher % positivity of BSI which might be due to their immature adaptive and native immune system, as described by Dash M. et al. [4] Seasonal variations in BSI are observed which showed a rise in positivity during July and August as compared to other months. Most infections culminate in India during rains due to water clogging, disease-ridden surroundings, etc. [7]

The higher occurrence of gram-negative bacteria (67.69%) than gram-positive bacteria (32.30%) was similar to most of the studies conducted in India and worldwide [5,6,23,2,3,4,7,8,9,10] *E. coli* was isolated more commonly in adult patients similar to studies conducted by *Pal N.* et al. [15] The organism is the most common cause of urinary tract infections and hence it can be more prevalent in BSI. The occurrence of MRSA

(98/1647) was considerable among gram-positive bacterial infections in adults. MRSA infections spread through skin-to-skin contact and can be associated with exposure to contaminated surfaces and infected people in crowds, unhygienic practices, etc. A significant number of *S. pneumoniae* infections was observed (78/1674) which was contradictory to some of the similar studies carried out in India denoting only higher Staphylococcal infections. [1,6,6,2,3,4,7,8,9,21] In our study, higher pneumococcal infections compared to other studies might be due to the quality guidelines followed by the laboratory and the instrument's sensitivity that can detect these fastidious fragile bacteria.

Enterobacterales showed resistance to almost all β-lactam antibiotics due to the production of β-lactamase. There is a slight rise in susceptibility when they are used with β- lactamase inhibitors (Clavulanic acid, Sulbactam). The isolates showed 67% susceptibility towards Carbapenems which was contradictory to studies carried out by N. Vasudeva, Banik, et al*.* showing high (75-100%) carbapenem sensitivity. *P*. *aeruginosa* and *A. baumanii* showed 55.9% and 58.4% sensitivity towards Imipenem and Meropenem. This was similar to the studies carried out in Sikkim, India by Tsering Yangzom et al. [5], and contradictory to the study- carried out by J. Sonawane et al*.* [9] showed high. Imipenem sensitivity (91.82%). Both bacteria exhibit β-lactamases and aminoglycoside-modifying enzymes, low permeability of outer membrane proteins, mutations in drug binding sites, and up-regulation of efflux pumps, etc. that make them intrinsically resistant to many antibiotics.

The present study shows a total of 30-41% of ESBL producing Gram-Negative bacteria including fermenters and non-fermenters which is consistent with the study carried out by J.P. Sonawane *et*.*al*.[10] and inconsistent with the study carried out by Pal N. et al*.* [15] (50-66%). Carbapenemase producers were 42-53% of Gram-negative fermenters and non-fermenters which is not consistent with the study carried out by J.P. Sonawane et al. [9] Antimicrobial resistance pattern varies concerning the rational or irrational use of antibiotics in those areas.

All gram-negative bacteria have shown higher susceptibility to colistin which is often used as a last resort. It is mostly used in combination with other drugs than used alone. As the drug is not frequently used over the other drugs, bacteria might not have developed resistance yet [24].

The most common Gram-positive bacteria- *S. aureus* has shown moderate to high susceptibility to all listed antibiotics like Vancomycin, Cephalosporins, Fluoroquinolones, Aminoglycosides, and cyclin group of antibiotics. *S. pneumoniae*, *S. pyogenes, and E. faecalis* showed high susceptibility to all listed antibiotics. No VRE was found in our study unlike the retrospective study published by T. Sering Yangzom et al*.* [22] The Gram-positive bacteria show less antimicrobial resistance patterns, usually. The reason is they lack an outer lipid membrane-like Gram-Negative bacteria, which helps in developing resistance by different mechanisms.

Though sepsis is fatal, the severity and death can be prevented with earlier diagnosis and appropriate targeted antimicrobial therapy. The available antimicrobial drugs are rapidly becoming ineffective because of indiscriminate usage. With effective and rationalized infection control practices for BSI, we can avoid the condition of pan drug resistance.

5. CONCLUSION

Sepsis needs precise, early diagnosis and treatment as it leads to fatality. Newly developing and emerging antibiotic-resistant strains are of major concern in sepsis management. The present study with the significant cohort provides information about BSI-causing bacteria and their AST profiles. Such laboratory studies will help understand local circulating strains, the emergence of new antibiotic resistance patterns, or any shift in the trends over a given period of time.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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