Egypt. J. Chem. **Vol. 67**, No. 2 pp. 91 - 102 (2024)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Evaluation of the VITEK®2 Cards for Rapid Direct Identification and Antimicrobial Susceptibility Testing of Human Pathogenic Bacteria

Yasser A. El-Ameir [1], Luay Y. El-hayyany [2], Ibrahim K. Ahmed [3], Awf A. Al-Rubaye [1], Alaa A. Fahmy [4, *], Yasameen Z. Khattab [5], Mohammed S. Sultan [1, *]

[1]*Botany Department, Faculty of Science, Mansoura University, Mansoura, 35516, Egypt*

[2]*General Directorate of Health in Anbar, Rutba, Anbar, Ministry of Health, Iraq*

[3]*Pharmacy Department Al-Rasheed University/College, Baghdad, Iraq*

[4]*Medical Surgical Nursing Department, Faculty of Nursing, Port Said University, Port Said, Egypt*

[5]*General Directorate of Health in Diyala, Diyala, Ministry of Health, Iraq*

Abstract

The VITEK®2 system may be used in this investigation to quickly identify bacteria and test them for susceptibility. Our goal was to analyse the extended spectrum isolating isolates problem causing infections in Mansoura Hospital, Egypt, throughout a 2-year period from February 2020 to October 2021. We also wanted to assess the bacterial profile and frequency of antibiotic resistance patterns of pathogens. Significant bacteremia was detected in 533 (2.563%) of the 21095 samples. A total of 533 isolates were examined; 502 (92%) of these were correctly recognized to the species level, while 31 (8%) of the isolates were not. VITEK®2 required 3 hours for direct identification reporting. The broth of the isolates was used to assess susceptibility to 8 antibiotics: ampicillin, cefotaxime, tetracycline, clindamycin, azithromycin, ofloxacin, gentamicin, and penicillin. With reporting times ranging from 2.6 to 16.4 h, the frequencies of susceptibility to the 8 antibiotics ranged from 75.5 to 82%, respectively. This approach can enable same-day reporting in contrast to conventional approaches that need one or two days, allowing for improved patient management. *Escherichia coli* made up 54 (26.6%) of hospital-acquired isolates and 35 (29.4%) of community-acquired isolates, while *Staphylococcus aureus* came in second with 33 (11.22%) of hospital-acquired isolates and 20 (17%) of community-acquired isolates, and *Staphylococcus epidermidis* came in third with 21 (7.14%) of hospital-acquired isolates and 18 (15 The 8 antibiotics studied showed high rates of resistance; 685 (30.6%) and 361 (18%) of gram-negative and gram-positive bacteria, respectively.

Keywords: Microbial identification; Susceptibility; Vitek II; Pathogenic bacteria; Antibiotics

1. Introduction

Infections of the bloodstream and urinary tract are a common bacterial infection that both general practitioners and hospital doctors face, a leading source of illness and mortality [1, 2]. Acute UTIs linked to significant morbidity and recurrent infection issues. According to studies, around 25% of women who have their initial UTI will have another incident in 180 days. Furthermore, UTIs are a common reason of septicemia, which leads to higher fatality rates, longer hospital stays, and higher healthcare expenses [3, 4].

The capacity to identify bacteria grown in blood cultures more quickly, as well as the subsequent adjustment of the right antibiotic prescription, is essential to improve the outcome of sepsis patients. Particularly in the outpatient setting, treatment must always start before the whole bacteriological results are available. Present information of the organisms that cause infection and their susceptibility to antibiotics is essential. Several factors affect how

*Corresponding author e-mail: mohammedsoltan915@gmail.com (Mohammed S. Sultan.).
Received date 01 June 2023; revised date 17 July 2023; accepted date 31 July 2023.
DOI: 10.21608/ejchem.2023.214813.8066

clinically bloodstream infections develop. Clinical management for the patient is significantly influenced by the type of bacteria involved and their susceptibility to antibiotics [5–9].

Due to their high prevalence and disastrous impact on mortality, morbidity, and cost, particularly in the case of nosocomial infections, bloodstream infections continue to be a major public health concern. Although prompt administration of an effective antibiotic regimen may reduce the length of hospitalization and mortality in patients with bloodstream infections, [10–12] delayed (and possibly less effective) treatment frequently leads to more advanced stages of bloodstream infection-related disease [13, 14]. Notably, septic shock, a particularly hazardous symptom of sepsis, is most frequently caused by drug-resistant and MDR pathogens, needing treatment within an hour of detection [15].

Accurate and rapid identification of the bloodstream infection causative agents and development of antibiotic susceptibility profiles are essential [16–18] for guiding efficient targeted antimicrobial treatment decisions. Reduced morbidity and mortality, fewer lab tests and procedures, quicker access to the right antimicrobial medication, shorter stays in the hospital and critical care units, and lower expenditures are all advantages for patients and the healthcare system [18–22].

One of the key responsibilities of the clinical microbiology laboratory is the detection of bloodstream infections. Rapid bacterial identification and susceptibility testing reduce expenses while improving patient care and outcomes [23–25].

Automated identification and susceptibility testing systems faced the challenge of changing their validated protocol from using overnight bacterial isolates taken from solid media to protocols allowing direct inoculation from positive blood cultures in order to reduce the amount of time required to obtain the results. As a result, there may be a chance that identification and susceptibility test results will be available the same day that a positive blood culture is discovered. The isolated colonies were then used for susceptibility testing and identification. The use of broad-spectrum antibiotics by doctors is influenced by rising rates of antibiotic resistance; there is little other option except to administer an empiric therapy prior to the identification of the infection's etiological agent [21, 26, 27].

Fast and perfect identification of gram-negative rods is critical for the therapy of illnesses caused by these bacteria, according to clinical microbiologists and clinicians. Only a handful of the automated identification techniques for gram-negative rods (and other bacteria) have been developed and made commercially available in recent years, including ATB, MicroScan, and VITEK. The new VITEK 2 system is significantly different from the previous VITEK system in that it provides definite identification findings for gram-negative rods (including Enterobacteriaceae and non-enteric bacilli) within 3 hours. This is due to modern technology based on fluorescence that is more sensitive to detecting metabolic changes and, as a result, enables noticeably quicker identifications through enhanced continuous monitoring of processes [28–30].

The market has long offered automated blood culture systems and automated bacterial identification and susceptibility testing systems [31]. New automated fluorescence-based fluorescence-based bacterial identification and susceptibility testing instrument, the VITEK 2 system, has shown promise in direct testing of positive blood cultures [19, 20, 32, 36-39]. Previous studies with pure bacterial cultures suggested that this technique could speed up the reporting of results by removing the need for overnight isolation of isolated colonies for rapid direct microbial identification from blood cultures and providing accurate identification and susceptibility data [18, 36, 40–43]. The study's aim was to recognize the spatial distribution of bacterial species in blood isolates and the pattern of those bacteria's antibiotic susceptibility.

2. Materials and Methods

2.1. Isolation and purification of bacteria

The isolation and purification of pathogenic bacteria done NA agar medium (1.25 gm peptone, 0.75 gm beef extract, 2 gm sodium chloride, 3.75 agar and 250 ml distilled water). The plates and the tubes incubated for 24h at 37°C.

2.2. Identification System

The filler-sealer unit, reader-incubator, computer control module, data terminal, and multi-copy printer make up the integrated VITEK 2's closed system. This method allows for the detection of chemical reactions and bacterial growth in the microwells of thin plastic cards.

The manufacturer advises using the most recent identity cards for gram-positive cocci (ID-GPC) and gram-negative bacilli (ID-GNB) that have been accepted for use with the VITEK 2 system for identification by the U.S. Food and Drug Administration. The 64-well ID-GNB included 41 tests total, including 18 tests each for sugar fermentation and absorption, urease, malonate utilisation, and tryptophane deaminase. There were also two tests each for ornithine and lysine decarboxylase. In the ID-GNB database, gram-negative rods were classified into 101 different taxa. Tests for motility, pigmentation, or indole were frequently added when requested by Vitek 2 to address

results showing a lack of differentiation. Sixteen fermentation tests, two decarboxylase tests (ornithine and arginine), twenty-two enzyme tests for aminopeptidases and aminopeptidases, two decarboxylase tests (pyruvate, optochin, novobiocin, polymyxin B sulphate, and 6.5 percent NaCl), and two enzymatic tests for aminopeptidases and aminopeptidases are among the forty-six tests in the 64-well ID- GPC. If recommended by Vitek2, an additional test for pigmentation conducted to address low discrimination.

A biohazard waste container used to dispose of all used playing cards. The most recent version of the VITEK 2 software (VT2-R02-02) used. Gram-negative bacilli represented by 101 distinct taxa in the ID-GNB database and gram-positive cocci by fifty different taxa in the ID-GPC database.

2.3. Antibacterial susceptibility testing

Results of the VITEK 2 direct susceptibility method and the broth microdilution method with pure cultures were compared in accordance with NCCLS recommendations were used to evaluate the susceptibility of bacterial isolates [44]. Ampicillin, cefotaxime, tetracycline, clindamycin, azithromycin, ofloxacin, gentamicin, penicillin were the eight antibiotics examined. Examples of variances in susceptibility that are classed as very big, major, or small include being resistant with the VITEK 2 system but sensitive by the reference technique, or being resistant with the VITEK 2 system but resistant by the reference method.

3. Results and Discussion

3.1. Isolation and purification of collected samples

Bloodstream infections are among the most severe and sometimes fatal infectious diseases, and they are most frequently seen in young children. Morbidity and mortality can be prevented by receiving early diagnosis and treatment [45]. Antimicrobial medication must typically be administered empirically to these patients. For a treatment to be effective, pathogen and antimicrobial resistance patterns must be accurately predicted [46]. Knowing the bacteria that thrive in hospitals is crucial for this reason [47]. 533 (2.53%) of the 21095 blood samples tested during the study period produced detectable germs. 255 (47.8%) of the 533 samples came from in-patients, and 278 (52.2%) came from outpatients. The majority of blood infection cases (21–55 years, 55%) were found in individuals who were young and middle-aged. 70 (16%) pediatric patients (16-20 years) and 168 (32%) elderly patients (60) made up the total number of infections. Blood infections were shown to occur far more frequently in females than in males, with 324 (61%) and 209 (39%), respectively (Table 1).

Table 1**.** Distribution of patients according to gender and age in a general Mansoura hospital in Egypt.

Gender	Age (years)					Total
	16-20	21-30	31-45	46-55	≥60	
Male	25 (36)	33 (33)	21 (35)	53 (39)	77 (42)	209 (39)
Female	45 (64)	67 (67)	39 (65)	82 (47)	91 (54)	324 (61)
Total	70 (13)	100 (19)	60 (11)	135 (25)	168 (32)	533 (100)

One of the most crucial procedures used to determine sepsis is blood culture. Our findings were analysed, and it was shown that considerable bacteriuria was present in 2.53% of the blood samples from inpatients and outpatients. Women made up the majority (61% of patients) and made up the majority of adult patients (87%), which supports a previous research indicating adult women had a higher prevalence than men, mostly for anatomic and physical reasons [48]. The prevalence in the current study was 2.53% (Table 1).

3.2. VITEK 2 system identification

Being able to report identification and susceptibility results directly from positive blood cultures as soon as they indicate positive for growth is very beneficial in reducing the time it takes to find the proper therapy. In order to identify gram-positive and gram-negative isolates from clinical samples within 3 hours, which may be clinically important, the VITEK 2 system combines a variety of advantages that may be of therapeutic significance. It has been demonstrated that prompt reporting of microbiology results to physicians lowers death rates significantly and promotes the earlier start of suitable antibiotic medication [24, 49]. According to findings from earlier investigations, the VITEK 2 system properly detected 85.3 to 100% of strains [40]. In our investigation, the isolates were identified by the VITEK 2 system 80% to 100%. However, from a clinical perspective, it should be kept in mind that the majority of *Serratia marcescens* isolates may be easily separated from similar species by straightforward additional tests. Of the *Serratia marcescens* isolates, 76% were identified with a poor level of discrimination (Table 2).

Gram-positive pathogens made up 253 (47.5%) of the pathogens, whereas Gram-negative pathogens made up 280 (52.5%) of the total. Table 2 presents a thorough examination of the etiological agents. In both outpatient and inpatient instances, *Escherichia coli*

was the most communal pathogen, represented for 35 (14.64%) and 54 (18.37%) of the causal agents, respectively. Following *E. coli, Staphylococcus aureus, Staphylococcus epidermidis, Clostridium tetani, Enterococcus spp. and Pseudomonas aeruginosa, Salmonella typhi, and Listeria monocytogenes, S. epidermidis* and *Enterobacter aerogenes* were the top blood-pathogens causing inpatients at our hospital, with 33 (11.22%), 21 (7.14%), 20 (6.80%), 19 (6.46%), and 18 (7.53%) respectively as shown in Table 2.

Table 2. Pathogenic bacteria isolated from the blood of inpatients and outpatients with infection.

Microorganisms	Number (%) of microorganisms isolated from blood			
	Inpatients		Outpatients	
	2020	2021	2020	2021
Gram-positive				
Listeria monocytogenes	4 (3)	7 (4.4)	12 (10.2)	7 (6)
Staphylococcus epidermidis	11 (8)	10 (6.3)	6 (5.1)	12 (10)
Staphylococcus xylosus	2 (1.5)	6 (4)	7 (6)	4 (3.3)
Staphylococcus hemolytic	5 (3.7)	9 (5.7)	3 (2.5)	10 (8.3)
Clostridium tetani	13 (9.5)	7 (4.4)	11 (9.3)	5 (4.1)
Enterococcus spp.	8 (6)	11 (7)	3 (2.5)	6 (5)
Staphylococcus aureus	12 (9)	21 (13.3)	13 (11)	7 (6)
Streptococcus pyogenes	6 (4.4)	3 (2)	8 (7)	4 (3.3)
Gram-negative				
Sphingomonas paucimobilis	7 (5.1)	5 (3.2)	2 (1.7)	2 (1.7)
Salmonella typhi	11 (8)	7 (4.4)	12 (10.2)	9 (7.4)
Escherichia coli	24 (17.6)	30 (19)	14 (12)	21 (17.4)
Klebsiella pneumonia	3 (2.2)	5 (3.2)	1 (0.8)	3 (2.5)
Pseudomonas aeruginosa	7 (5.1)	12 (7.6)	6 (5.1)	8 (6.6)
Haemophilus influenzae	5 (3.7)	2 (1.3)	2 (1.7)	1 (0.8)
Acinetobacter spp.	3 (2.2)	1 (0.6)	5 (5.1)	1 (0.8)
Enterobacter aerogenes	2 (1.5)	5 (3.2)	7 (6)	11 (9.1)
Serratia marcescens	4 (3)	8 (5.1)	2 (1.7)	3 (2.5)
Proteus spp.	3 (2.2)	7 (4.4)	1 (0.8)	2 (1.7)
Bacteroides fragilis	6 (4.4)	2 (1.3)	3 (2.5)	5 (4.1)
Total	136	158	118	121

90% of Gram-positive bacteria and 91% of Gram-negative are correctly identified on average at the species level. In comparison to Gram-negative, Gram-positive have a higher identification rate. We assessed eight gram-positive and eleven gram-negative species commonly encountered in the clinic, each with 10 or 89 bacterial strains. The system determines that the identification is correct for bacterial species for which the accuracy of identification is more than 90%. The system determines that the identification is correct for bacterial species for which the accuracy of identification is more than 90%. 502 out of the 533 bacterial samples that were evaluated had the right identification. The correct identification rates are 100% for *L. monocytogenes, S. xylosus, S. aureus, S. typhi, E. coli*, and *Haemophilus influenzae*; 96% for *S. hemolytic*; 95% for *S. epidermidis, Strep. pyogenes*, and 94% for *C. tetani*; 92% for *K. pneumonia* and *Proteus* spp., 88% for *P. aeruginosa*. The remaining 31 samples were deemed unsuccessful because the identification accuracy fell below 90%. (Table 3).

Salmonella spp., S. aureus, Klebsiella, and *Streptococci* species, in that order, were most often isolated in blood cultures at Gaziantep Children's Hospital [50]. *E. coli* and *Klebsiella* sp. were the most frequently isolated germs in a different investigation. The most frequent isolates, according to Birol *et al.*, were 1000 *Staphylococci* spp. (35.6%), 782 *S. aureus* (27.8%), and 303 *E. coli* (10.8%) [51]. Developing bacteria differ amongst hospitals. Patients in Egypt with bloodstream infections participated in this study. Isolated microorganisms vary among regions, as

shown in the investigations. In this study, *E. coli* (16.7%), *S. aureus* (9.94%), *S. typhi* (7.31%), *S. epidermidis* (7.31%), *C. tetani* (6.75%), *P. aeruginosa* (6.2%), and *L. monocytogenes* (5.62%) were the most frequently isolated microorganisms. standard practice (>96 % both for Gram-positive and Gram-negative) (Table 3). Using VITEK 2, similar outcomes for direct susceptibility have also been reported by [36, 38].

According to a study on nosocomial blood toxicities in Brazilian paediatric patients, *Staphylococci* (21.3%), *Klebsiella* spp. (15.7%), *S. aureus* (10.6%), and *Acinetobacter* spp. (9.2%) were the most frequently isolated pathogens [52]. The most frequent cause of nosocomial bloodstream infections, according to reports, is *S. aureus*, followed by *K. pneumoniae* and *Staphylococci* sp. [53]. According to our statistics, *E. coli* continues to be the blood bacterium that causes sepsis most frequently in both community and hospital settings. Our results are therefore in line with those of other research [54] in which *E. coli* was the most common pathogen recovered from both inpatients and outpatients. Additionally, *S. aureus* was found to be the second most frequent isolate from patients in our investigation, which is consistent with data from other studies that have reported [55] (Table 3).

Table 3. Identification rates of bacterial identification from outpatients vs. inpatients in Mansoura Hospital.

Organism	No. of tested isolates	No. (%) of correctly identified isolates
Gram-positive		
Listeria monocytogenes	30	30 (100)
Staphylococcus epidermidis	39	37 (95)
Staphylococcus xylosus	19	19 (100)
Staphylococcus hemolytic	27	26 (96)
Clostridium tetani	36	34 (94)
Enterococcus spp.	28	24 (86)
Staphylococcus aureus	53	53 (100)
Streptococcus pyogenes	21	20 (95)
Gram-negative		
Sphingomonas paucimobilis	16	13 (81)
Salmonella typhi	39	39 (100)
Escherichia coli	89	89 (100)
Klebsiella pneumonia	12	11 (92)
Pseudomonas aeruginosa	33	29 (88)
Haemophilus influenzae	10	10 (100)
Acinetobacter spp.	10	8 (80)
Enterobacter aerogenes	25	22 (88)
Serratia marcescens	17	13 (76)
Proteus spp.	13	12 (92)
Bacteroides fragilis	16	13 (81)
Total	533	502 4)

3.3. VITEK 2 direct susceptibility test

The differences in antibiotic susceptibility between isolates from community patients and hospital patients may be caused by the presence of extra risk factors for antibiotic resistance in the hospital population. Frequent use of antibiotics, underlying disease, and the presence of intrusive equipment are a few of these. Alarmingly high levels of resistance to various routinely used antibiotics have been found in *E. coli* and other bacteria. For instance, the level of *E. coli* resistance to routinely used oral antibiotics among inpatients and outpatients is very high. *E. coli* had substantially greater levels of fluoroquinolone resistance than those found in recent investigations conducted in Kuwait [56], Europe, and Canada [57]. The recent recognition of fluoroquinolone exposure as a separate threat factor for ciprofloxacin-resistant *E. coli* from in patients [58] may have contributed to this high degree of resistance. One of the antibiotics that general practitioners in Mansoura most frequently prescribe is ciprofloxacin. According to Tables 4 and 5, our study demonstrates that the prevalence of *E. coli* is higher in Mansoura Hospital than in other countries in the region [59, 60].

Table 4. Frequency and percentage of resistant Gram-positive pathogens isolated from outpatients vs. inpatients in Mansoura Hospital.

Pathogen	Year	Total No. of isolates Out/In	Percentage of Out vs. In bacteria resistant to							
			AMP	CTX	TCN	CM	AZI	OFX	GM	PCN
L. monocytogenes	2020	12/4	-	-	12/11	-	5/8	7/6	23/20	19/23
	2021	7/7	-	-	8/13	-	7/10	5/8	21/18	21/25
		19/11	-	-	10/12	-	6/9	6/7	22/19	20/24
S. epidermidis	2020	6/11	11/7	6/14	20/24	-	12/16	16/21	17/15	18/21
	2021	12/10	13/9	10/12	26/18	-	28/24	22/27	23/27	16/23
		18/21	12/8	8/13	23/21	-	20/20	19/24	20/21	17/22
S. xylosus	2020	7/2	27/23	15/17	20/21	19/18	21/23	16/25	11/19	13/11
	2021	4/6	29/27	25/23	18/29	11/16	19/21	18/11	21/27	17/15
		11/8	28/25	20/20	19/25	20/17	20/22	16/18	16/23	15/13
S. hemolytic	2020	3/5	11/13	28/20	24/21	8/6	22/19	23/21	6/9	6/11
	2021	10/9	21/23	24/24	20/25	6/6	20/19	23/27	14/21	10/13
		13/14	16/18	26/22	22/23	7/6	21/19	23/24	10/15	8/12
C. tetani	2020	11/13	7/12	8/9	6/10	5/5	7/6	5/9	5/8	10/13
	2021	5/7	13/16	6/7	8/12	7/5	9/8	15/13	7/6	12/15
		16/20	10/14	7/8	7/11	6/5	8/7	10/11	6/7	11/14
Enterococcus spp.	2020	3/8	10/13	-	5/7	-	23/20	-	10/13	24/23
	2021	6/11	12/7	-	9/11	-	19/22	-	12/15	26/25
		9/19	11/10	-	7/9	-	21/21	-	11/14	25/24
S. aureus	2020	13/12	-	20/23	-	10/8	20/19	20/23	21/24	80/93
	2021	7/21	-	22/19	-	12/10	22/21	24/17	23/22	84/89
		20/33	-	21/21	-	11/9	21/20	22/20	22/23	82/91
Strep. pyogenes	2020	8/6	-	18/16	-	29/27	21/26	14/12	9/5	16/19
	2021	4/3	-	22/26	-	31/29	19/18	10/16	13/15	18/13
		12/9	-	20/21	-	30/28	20/22	12/14	11/10	17/16

AMP: Ampicillin, CTX: Cefotaxime, TCN: Tetracycline, CM: Clindamycin, AZI: Azithromycin, OFX: Ofloxacin, GM: Gentamicin, PCN: Penicillin.

The susceptibility of the Gram-positive and Gram-negative isolates is shown as resistance rates (Tables 4 and 5). Gram-negative bacteria from inpatients were typically more resistant to antimicrobials than those from outpatients. Table 4 lists the frequencies of resistance for gram-positive bacterial isolates. Azithromycin, gentamicin, and penicillin were all effective treatments for the gram-positive isolates. None of the *L. monocytogenes*, *S. aureus*, and *Strep. pyogenes* isolates were resistant to ampicillin; *L. monocytogenes* and *Enterococcus* spp. isolates were resistant to cefotaxime; *S. aureus*, and *Strep. pyogenes* isolates were resistant to tetracycline, *L. monocytogenes*, *S. epidermidis*, and *Enterococcus* spp. isolates were resistant to clindamycin; *Enterococcus* spp. isolates were resistant to ofloxacin. The resistance percentages of Gram-negative isolates are displayed in Table 5.

Table 5. Frequency and percentage of resistant Gram-negative pathogens isolated from outpatients vs. inpatients in Mansoura Hospital.

Pathogen	Year	Total No. of isolates Out/In	Percentage of Out vs. In bacteria resistant to							
			AMP	CTX	TCN	CM	AZI	OFX	GM	PCN
S. paucimobilis	2020	2/7	11/10	9/12	-	-	11/13	-	12/10	9/13
	2021	2/5	13/10	7/10	-	-	15/17	-	16/12	11/13
		4/12	12/10	8/11	-	-	13/15	-	14/11	10/13
S. typhi	2020	12/11	17/15	7/9	-	-	-	-	-	5/6
	2021	9/7	9/11	13/13	-	-	-	-	-	7/4
		21/18	13/13	10/11	-	-	-	-	-	6/5
E. coli	2020	14/24	62/72	11/23	22/21	-	24/20	27/25	11/14	6/5
	2021	21/30	60/74	13/21	24/23	-	18/20	23/21	9/12	8/7

		35/54	61/73	12/22	23/22	-	21/20	25/23	10/13	7/6
	2020	1/3	9/12	22/20	19/23	5/6	11/10	19/17	-	16/11
K. pneumonia	2021	3/5	11/14	18/24	21/17	5/4	13/12	21/25	-	14/15
		4/8	10/13	20/22	20/20	5/5	12/11	20/22	-	15/13
	2020	6/7	-	-	-	-	20/19	6/7	-	15/14
P. aeruginosa	2021	8/12	-	-	-	-	16/15	4/11	-	13/12
		14/19	-	-	-	-	13/12	10/9	-	14/14
	2020	2/5	-	11/9	-	5/7	6/12	-	-	10/11
H. influenzae	2021	1/ 2	-	13/11	-	7/9	14/8	-	-	10/13
		3/7	-	12/10	-	6/8	10/10	-	-	10/12
	2020	5/3	-	9/12	-	19/23	5/6	11/10	19/17	16/11
Acinetobacter spp.	2021	1/1	-	11/14	-	21/17	5/4	13/12	21/25	14/15
		6/4	-	10/13	-	20/20	5/5	12/11	20/22	15/13
	2020	7/2	7/11	15/13	-	11/12	10/13	17/20	12/10	10/8
E. aerogenes	2021	11/5	13/11	7/7	-	13/10	14/15	13/10	14/8	12/6
		18/7	10/11	11/10	-	12/11	12/14	15/15	13/9	11/7
	2020	2/4	9/12	6/9	10/12	8/11	16/12	10/13	-	13/10
S. marcescens	2021	3/8	11/14	8/9	10/8	10/5	10/14	12/11	-	11/10
		5/12	10/13	6/9	10/10	9/8	13/13	11/12	-	12/10
	2020	1/3	-	-	9/12	22/20	19/23	5/6	11/10	19/17
Proteus spp.	2021	2/7	-	-	11/14	18/24	21/17	5/4	13/12	21/25
		3/10	-	-	10/13	20/22	20/20	5/5	12/11	20/22
	2020	3/6	-	12/15	20/17	8/113	-	-	6/9	12/11
B. fragilis	2021	5/2	-	12/13	16/17	12/11	-	-	4/5	8/9
		8/8	-	12/14	13/14	10/12	-	-	5/7	10/10

MP: Ampicillin, CTX: Cefotaxime, TCN: Tetracycline, CM: Clindamycin, AZI: Azithromycin, OFX: Ofloxacin, GM: Gentamicin, PCN: Penicillin.

All the Gram-negative isolates were susceptible to penicillin. No one of the *P. aeruginosa*, *H. influenzae*, *Acinetobacter* spp., *Proteus* spp., and *B. fragilis* isolates were resistant to ampicillin; *P. aeruginosa* and *Proteus* spp. isolates were resistant to cefotaxime; *S. paucimobilis*, *S. typhi*, *P. aeruginosa*, *H. influenzae*, *Acinetobacter* spp., *E. aerogenes*, and *Proteus* spp. isolates were resistant to tetracycline; *S. paucimobilis*, *S. typhi*, *E. coli*, and *P. aeruginosa* isolates were resistant to clindamycin; *P. aeruginosa* and *Proteus* spp. isolates were resistant to cefotaxime; *S. typhi* and *B. fragilis* isolates were resistant to azithromycin; *P. aeruginosa*, *S. typhi*, and *B. fragilis* isolates were resistant to ofloxacin; *S. typhi*, *K. pneumonia*, *P. aeruginosa*, *H. influenzae*, and *S. marcescens* isolates were resistant to gentamicin (Table 5).

Our findings indicated a marked decline in susceptibility to common community antibiotics. For many of the blood pathogens isolated in this investigation, ampicillin, tetracycline, clindamycin, ofloxacin, and gentamicin did not provide adequate in vitro coverage. As empirical therapy choices in an outpatient departmental environment, they are therefore not very useful. The only medications that continue to be effective against the majority of blood pathogens and can be used as initial treatment for mild sepsis, particularly in the community, are cefotaxime, azithromycin, and penicillin (Tables 4 and 5The current findings might be an indication of our region's increased usage of prescribed drugs to treat diseases picked up in hospitals or the community, like sepsis or respiratory tract infections. This excessive use of antibiotics may favour phenotypes of multidrug-resistant E. coli, which have the potential to spread throughout our region. In our region, additional community-level investigations on antibiotic usage are required to confirm this presumption. In general, the blood pathogens isolated in this investigation were effectively covered by the in vitro activity of the drugs gentamicin, cefotaxime, azithromycin, and penicillin. For very unwell hospital patients with suspected sepsis, this information will be helpful in selecting empiric therapy (Table 6).

Table 6. Diagnostic accuracy of the VITEK 2 system for detection of resistance to 8 antibiotics with pathogenic isolates gram-positive (n = 253), and gram-negative (n = 280).

Antibacterial agents	No. of antibacterial tests	Sensitivity	Resistance
	Gram-positive		

Ampicillin	2024	104	41.1%	149	58.9%
Cefotaxime		58	23%	195	77%
Tetracycline		74	29.2%	179	7.8%
Clindamycin		97	38.3%	156	3%
Azithromycin		253	100%	NA	NA
Ofloxacin		28	11.1%	225	88.9%
Gentamicin		253	100%	NA	NA
Penicillin		253	100%	NA	NA
Total		1663	82%	361	18%
Gram-negative					
Ampicillin	2240	82	28.3%	198	71.7%
Cefotaxime		46	16.4%	234	83.6%
Tetracycline		133	47.5%	147	52.5%
Clindamycin		177	63.2%	108	36.8%
Azithromycin		55	19.6%	225	80.4%
Ofloxacin		81	29%	199	71%
Gentamicin		111	39.6%	169	60.4%
Penicillin		280	100%	NA	NA
Total		1555	69.4%	685	30.6%
Overall	4264	3218	75.5%	1046	24.5%

The VITEK 2 also showed excellent accuracy for detection of resistant Gram-positive isolates (82% sensitivity and 18% Resistance) and resistant Gram-negative isolates (69.4% sensitivity and 30.6% Resistance), as well as the resistance and sensitivity degrees of Gram-positive isolates shown in Table 6. Ampicillin was sensitivity rate for 104 strains with 41.1% and resistant rate for 149 strains with 58.9%. Cefotaxime was sensitivity rate for fifty-eight strains with 23% and resistant rate for 195 strains with 77%. Tetracycline was sensitivity rate for seventy-four strains with 29.2% and resistant rate for 179 strains with 7.8%. Clindamycin was sensitivity rate for ninety-seven strains with 38.3% and resistant rate for 156 strains with 3%. Ofloxacin was sensitivity rate for twenty-eight strains with11.1% and resistant rate for 225 strains with 88.9%. While azithromycin, gentamicin, and penicillin were sensitivity rate for 253 strains with 100% and no resistant rate had detected (Table 6).

The resistance and sensitivity degrees of Gram-negative bacterial isolates shown in Table 6. Ampicillin was sensitivity rate for eighty-two strains with 28.3% and resistant rate for 198 strains with 71.7%. Cefotaxime was sensitivity rate for forty-six strains with 16.4% and resistant rate for 234 strains with 83.6%. Tetracycline was sensitivity rate for 133 strains with 47.5% and resistant rate for 147 strains with 52.5%. Clindamycin was sensitivity rate for 177 strains with 63.2% and resistant rate for 108 strains with 38.8%. Azithromycin was sensitivity rate for fifty-five strains with 19.6% and resistant rate for 225 strains with 80.4%. Ofloxacin was sensitivity rate for eighty-one strains with 29% and resistant rate for 199 strains with 81%. Gentamicin was sensitivity rate for 111 strains with 39.6% and resistant rate for 169 strains with 60.4%. Penicillin was sensitivity rate for 280 strains with 100% and no resistant rate had detected (Table 6). There may be a number of variables that contribute to the increased prevalence of bacteria as a cause of sepsis, including the kind of patients, advancements in patient surgical and medical management, excessive use of broad-spectrum antibiotics, and a high prevalence of diabetes mellitus and obesity [61]. An established risk factor for adult *S. aureus* infection, diabetes mellitus was present in 36% of the sepsis patients in a prior investigation. Additionally, prior research indicates that S. aureus colonises the vagina of both pregnant and non-pregnant people at a significant rate [62]. Gram-negative bacterial resistance rates were often lower in outpatients than inpatients, which is consistent with observations made across the globe [63, 64] (Table 6).

Table 7. Comparison of direct susceptibility testing of bacteria with the standard approach.

Organism	No. of tested isolates	No. (%) of correctly identified isolates	Antibacterial tests	No. (%) of Agreements with standard	No. (%) of Minor errors	No. (%) of Major errors	No. (%) of Very major errors
Gram-positive	253	243	2024	1663 (81)	301 (15)	30 (2)	30 (2)
L. monocytogenes	30	30 (100)	240	150 (7.4)	83 (4.1)	4 (0.2)	2 (0.1)

S. epidermidis	39	37 (95)	312	273 (13.5)	33 (1.6)	3 (0.15)	3 (0.15)
S. xylosus	19	19 (100)	152	152 (7.5)	0	0	0
S. hemolytic	27	26 (96)	216	216 (11)	0	0	0
C. tetani	36	34 (94)	288	288 (14.2)	0	0	0
Enterococcus spp.	28	24 (86)	224	140 (7)	71 (3.5)	10 (0.5)	1 (0.05)
S. aureus	53	53 (100)	424	318 (15.7)	96 (4.7)	5 (0.25)	5 (0.25)
Strep. pyogenes	21	20 (95)	168	126 (6.2)	39 (2)	1 (0.05)	2 (0.1)
Gram-negative	280	259	2240	1555 (69.4)	655 (29.2)	18 (0.8)	12 (0.5)
S. paucimobilis	16	13 (81)	128	80 (3.6)	44 (2)	2 (0.1)	2 (0.1)
S. typhi	39	39 (100)	312	117 (5.2)	189 (8.4)	3 (0.13)	3 (0.13)
E. coli	89	89 (100)	712	623 (28)	87 (4)	1 (0.04)	1 (0.04)
K. pneumonia	12	11 (92)	96	84 (3.75)	11 (0.5)	1 (0.04)	0
P. aeruginosa	33	29 (88)	264	99 (4.4)	157 (7)	5 (0.22)	3 (0.13)
H. influenzae	10	10 (100)	80	40 (1.8)	37 (1.7)	1 (0.04)	2 (0.1)
Acinetobacter spp.	10	8 (80)	80	60 (2.7)	18 (1)	1 (0.04)	1 (0.04)
E. aerogenes	25	22 (88)	200	175 (8)	21 (0.9)	2 (0.1)	2 (0.1)
S. marcescens	17	13 (76)	136	119 (5.3)	13 (0.6)	2 (0.1)	2 (0.1)
Proteus spp.	13	12 (92)	104	78 (3.5)	23 (1.03)	2 (0.1)	1 (0.04)
B. fragilis	16	13 (81)	128	80 (3.6)	42 (2)	2 (0.1)	3 (0.13)
Total	533	502 (94)	4264	3218 (0.75)	998 (23.4)	41 (1)	7 (0.2)

502 (94%) of the 533 gram-positive and gram-negative bloodstream isolates were successfully identified by the VITEK 2 equipment. Gram-negative isolates were (n = 31) while unidentified gram-positive isolates were (n = 10). 94% of isolates were successfully identified following repeated testing, with findings being provided after times ranging from 1 hour 42 minutes to 5 hours 33 minutes (median, 2 h 20 min). Of the 253 Gram-positive bacterial strains utilised for direct VITEK 2 testing that were consecutively collected, identified at the species level, and tested. The distribution of category agreement and error rates between the two approaches is presented in Table 7, and results are contrasted to those from the traditional culture-dependent VITEK 2 AST method. The samples underwent 2024 antimicrobial tests in all. According to Table 7, the two approaches had an overall category agreement rate of 81% (1663/2024), with minor error rates of 15% (301/2024), major error rates of 2% (30/2024), and very significant error rates of 2% (30/2024). Additionally, 280 Gram-negative strains at the species level were isolated and used for direct AST analysis on VITEK 2. Table 7 shows the distribution of group agreement and error degrees for the direct and culture-dependent methods. 2240 antimicrobial tests were conducted on the Gram-negative material in total. As indicated in Table 7, there was a 69.2% (1555/2240) overall category agreement, with rates for minor mistakes of 29.2% (655/2240), significant errors of 0.8% (18/2240), and very major errors of 0.5% (12/2240).

4. Conclusions

We are aware that the majority of isolates from the community that are evaluated in our laboratory and many blood infections treated with bacteriological testing may have originated from patients whose previous antimicrobial treatments had unsuccessful from patients with additional causal threat issues. Therefore, the findings of our investigation could not accurately reflect the dispersal and pattern of antibiotic resistance of the blood pathogens causing acute, simple infections and might not always be used as a foundation for developing recommendations for the empirical management of sepsis. However, they underline the need for further research into the distribution and susceptibility of microorganisms causing simple sepsis, which should reveal the best antibiotic to use as an empirical treatment. The findings of our study also improved our understanding of the pathogen kinds and patterns of resistance to antibiotic medications that cause blood infections in hospitalized patients who are both inpatients and outpatients. In the hospital context, in particular, this knowledge would aid clinicians in selecting the best empirical treatment.

Conflicts of interest

"There are no conflicts to declare".

Acknowledgments

"None"

5. References

[1] Voidazan, S., et al., Healthcare associated infections-a new pathology in medical practice? International journal of environmental research and public health, 2020. 17(3): p. 760.

[2] Roth, F., et al., Clinical and Financial Impact of Rapid Antimicrobial Susceptibility Testing in Blood Cultures. Antibiotics, 2022. 11(2): p. 122.

[3] Nguyen, S.N., et al., Clinical Epidemiology Characteristics and Antibiotic Resistance Associated with Urinary Tract Infections Caused

by E. coli. International Journal of Nephrology, 2022. 2022.
[4] Zilberberg, M.D., et al. Descriptive Epidemiology and Outcomes of Hospitalizations with Complicated Urinary Tract Infections in the United States, 2018. in Open Forum Infectious Diseases. 2022. Oxford University Press US.
[5] Harbarth, S., V. Nobr, and D. Pittet, Does antibiotic selection impact patient outcome? Clinical infectious diseases, 2007. 44(1): p. 87-93.
[6] Kollef, M.H., Broad-spectrum antimicrobials and the treatment of serious bacterial infections: getting it right up front. Clinical Infectious Diseases, 2008. 47(Supplement_1): p. S3-S13.
[7] Cowart, M.C., T.S. Heath, and A. Shipman, The Effect of Rapid Initiation Versus Delayed Initiation of Antibiotics in Pediatric Patients with Sepsis. The Journal of Pediatric Pharmacology and Therapeutics, 2022. 27(1): p. 45-50.
[8] Dunne, M.W., et al., Impact of Empirical Antibiotic Therapy on Outcomes of Outpatient Urinary Tract Infection Due to Nonsusceptible Enterobacterales. Microbiology spectrum, 2022. 10(1): p. e02359-21.
[9] Kang, A., R. Beuttler, and E. Minejima, Evaluation of step-down oral antibiotic therapy for uncomplicated streptococcal bloodstream infections on clinical outcomes. Therapeutic Advances in Infectious Disease, 2022. 9: p. 20499361211073248.
[10] Vrijens, F., et al., Hospital-acquired, laboratory-confirmed bloodstream infections: linking national surveillance data to clinical and financial hospital data to estimate increased length of stay and healthcare costs. Journal of Hospital Infection, 2010. 75(3): p. 158-162.
[11] Lee, C.-C., et al., Timing of appropriate empirical antimicrobial administration and outcome of adults with community-onset bacteremia. Critical Care, 2017. 21(1): p. 1-9.
[12] Lee, C.-C., et al., Prognostic Effects of Delayed Administration of Antimicrobial Therapy in Older Persons Experiencing Bacteremia with or Without Initial Sepsis Presentations. Journal of the American Medical Directors Association, 2022. 23(1): p. 73-80.
[13] Rhodes, A., et al., Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med. 2017.
[14] Lin, C.-H., et al., Effects of Inappropriate Empirical Antimicrobial Therapy on the Outcomes of Patients with Community-Onset Bacteremia: Age Matters. 2021.
[15] Gaieski, D.F., et al., Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department. Critical care medicine, 2010. 38(4): p. 1045-1053.
[16] Munson, E.L., et al., Detection and treatment of bloodstream infection: laboratory reporting and antimicrobial management. Journal of clinical microbiology, 2003. 41(1): p. 495-497.
[17] Fothergill, A., et al., Rapid identification of bacteria and yeasts from positive-blood-culture bottles by using a lysis-filtration method and matrix-assisted laser desorption ionization–time of flight mass spectrum analysis with the SARAMIS database. Journal of clinical microbiology, 2013. 51(3): p. 805-809.
[18] Burillo, A., et al., Gram-stain plus MALDI-TOF MS (Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry) for a rapid diagnosis of urinary tract infection. PLoS One, 2014. 9(1): p. e86915.
[19] Kerremans, J., et al., Rapid identification and antimicrobial susceptibility testing reduce antibiotic use and accelerate pathogen-directed antibiotic use. Journal of antimicrobial chemotherapy, 2008. 61(2): p. 428-435.
[20] Gherardi, G., et al., Comparative evaluation of the Vitek-2 Compact and Phoenix systems for rapid identification and antibiotic susceptibility testing directly from blood cultures of Gram-negative and Gram-positive isolates. Diagnostic microbiology and infectious disease, 2012. 72(1): p. 20-31.
[21] Perez, K.K., et al., Integrating rapid pathogen identification and antimicrobial stewardship significantly decreases hospital costs. Archives of Pathology and Laboratory Medicine, 2013. 137(9): p. 1247-1254.
[22] Sheth, S., et al., Pharmacist-driven implementation of fast identification and antimicrobial susceptibility testing improves outcomes for patients with Gram-negative bacteremia and candidemia. Antimicrobial agents and chemotherapy, 2020. 64(9): p. e00578-20.
[23] Trenholme, G., et al., Clinical impact of rapid identification and susceptibility testing of bacterial blood culture isolates. Journal of Clinical Microbiology, 1989. 27(6): p. 1342-1345.
[24] Doern, G.V., et al., Clinical impact of rapid in vitro susceptibility testing and bacterial identification. Journal of clinical microbiology, 1994. 32(7): p. 1757-1762.
[25] Weinstein, M.P., et al., The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of

bacteremia and fungemia in adults. Clinical Infectious Diseases, 1997. 24(4): p. 584-602.
[26] Ibrahim, E.H., et al., The influence of inadequate antimicrobial treatment of bloodstream infections on patient outcomes in the ICU setting. Chest, 2000. 118(1): p. 146-155.
[27] Harbarth, S., et al., Inappropriate initial antimicrobial therapy and its effect on survival in a clinical trial of immunomodulating therapy for severe sepsis. The American journal of medicine, 2003. 115(7): p. 529-535.
[28] Gayral, J., R. Robinson, and D. Sandstedt, A new integrated system for microbiological testing: the Vitek II system, abstr. P254. Clin. Microbiol. Infect, 1997. 3(Suppl 2): p. 53.
[29] Ullberg, M. and V. Özenci, Identification and antimicrobial susceptibility testing of Gram-positive and Gram-negative bacteria from positive blood cultures using the Accelerate Pheno™ system. European Journal of Clinical Microbiology & Infectious Diseases, 2020. 39(1): p. 139-149.
[30] Zhu, Y., et al., Evaluation of the clinical systems for polymyxin susceptibility testing of clinical Gram-negative bacteria in China. Frontiers in Microbiology, 2021. 11: p. 610604.
[31] Jossart, M.-F. and R. Courcol, Evaluation of an automated system for identification of Enterobacteriaceae and nonfermenting bacilli. European Journal of Clinical Microbiology and Infectious Diseases, 1999. 18(12): p. 902-907.
[32] Ling, T.K., Z. Liu, and A.F. Cheng, Evaluation of the VITEK 2 system for rapid direct identification and susceptibility testing of gram-negative bacilli from positive blood cultures. Journal of clinical microbiology, 2003. 41(10): p. 4705-4707.
[33] Nonhoff, C., S. Rottiers, and M. Struelens, Evaluation of the Vitek 2 system for identification and antimicrobial susceptibility testing of Staphylococcus spp. Clinical microbiology and infection, 2005. 11(2): p. 150-153.
[34] Mittman, S.A., et al., Comparison of BD Phoenix to Vitek 2, MicroScan MICroSTREP, and Etest for antimicrobial susceptibility testing of Streptococcus pneumoniae. Journal of clinical microbiology, 2009. 47(11): p. 3557-3561.
[35] Wimmer, J.L., et al., Strategy for rapid identification and antibiotic susceptibility testing of gram-negative bacteria directly recovered from positive blood cultures using the Bruker MALDI Biotyper and the BD Phoenix system. Journal of clinical microbiology, 2012. 50(7): p. 2452-2454.
[36] Machen, A., T. Drake, and Y.F. Wang, Same day identification and full panel antimicrobial susceptibility testing of bacteria from positive blood culture bottles made possible by a combined lysis-filtration method with MALDI-TOF VITEK mass spectrometry and the VITEK2 system. PloS one, 2014. 9(2): p. e87870.
[37] Chen, J.-R., et al., Rapid identification and susceptibility testing using the VITEK 2 system using culture fluids from positive BacT/ALERT blood cultures. J Microbiol Immunol Infect, 2008. 41(3): p. 259-64.
[38] Romero-Gómez, M.-P., et al., Identification and susceptibility testing of microorganism by direct inoculation from positive blood culture bottles by combining MALDI-TOF and Vitek-2 Compact is rapid and effective. Journal of Infection, 2012. 65(6): p. 513-520.
[39] Prod'hom, G., C. Durussel, and G. Greub, A simple blood-culture bacterial pellet preparation for faster accurate direct bacterial identification and antibiotic susceptibility testing with the VITEK 2 system. Journal of medical microbiology, 2013. 62(Pt 5): p. 773-777.
[40] Funke, G., et al., Evaluation of the VITEK 2 system for rapid identification of medically relevant gram-negative rods. Journal of clinical microbiology, 1998. 36(7): p. 1948-1952.
[41] Ling, T.K., et al., Evaluation of VITEK 2 rapid identification and susceptibility testing system against gram-negative clinical isolates. Journal of clinical microbiology, 2001. 39(8): p. 2964-2966.
[42] Gavin, P., et al., Evaluation of the Vitek 2 system for rapid identification of clinical isolates of gram-negative bacilli and members of the family Streptococcaceae. European Journal of Clinical Microbiology and Infectious Diseases, 2002. 21(12): p. 869-874.
[43] Schneiderhan, W., et al., Work flow analysis of around-the-clock processing of blood culture samples and integrated MALDI-TOF mass spectrometry analysis for the diagnosis of bloodstream infections. Clinical chemistry, 2013. 59(11): p. 1649-1656.
[44] Wayne, P., National committee for clinical laboratory standards. Performance standards for antimicrobial disc susceptibility testing, 2002. 12: p. 01-53.
[45] Gray, J., S. Gossain, and K. Morris, Three-year survey of bacteremia and fungemia in a pediatric intensive care unit. The Pediatric infectious disease journal, 2001. 20(4): p. 416-421.
[46] Berner, R., et al., Bacteremic episodes in pediatric oncologic patients, especially caused by the Streptococcus viridans group. Klinische Padiatrie, 1998. 210(4): p. 256-260.
[47] Xiao, X., Z.-C. Wu, and K.-C. Chou, A., multi-label classifier for predicting the subcellular localization of gram-negative bacterial proteins

with both single and multiple sites. PloS one, 2011. 6(6): p. e20592.
[48] Topley, W.W.C., Topley and Wilson's microbiology and microbial infections. 1998: Arnold.
[49] Barenfanger, J., C. Drake, and G. Kacich, Clinical and financial benefits of rapid bacterial identification and antimicrobial susceptibility testing. Journal of clinical microbiology, 1999. 37(5): p. 1415-1418.
[50] Yiş, R., Güneydoğu Anadolu Bölgesi'nde bir çocuk hastanesinde kan kültürü sonuçlarının değerlendirilmesi. Türk Pediatr Arş, 2015. 50(2): p. 102-7.
[51] Yılmaz, S., et al., İki yıllık dönemde kan kültürlerinden izole edilen mikroorganizmalar ve antibiyotik duyarlılıkların değerlendirilmesi. Gülhane Tıp Derg, 2013. 55(4): p. 247-52.
[52] Eaton, S.L., et al., Total protein analysis as a reliable loading control for quantitative fluorescent Western blotting. PloS one, 2013. 8(8): p. e72457.
[53] Jaballah, N.B., et al., Epidemiology of hospital-acquired bloodstream infections in a Tunisian pediatric intensive care unit: a 2-year prospective study. American journal of infection control, 2007. 35(9): p. 613-618.
[54] Krawczyk, B., et al., Characterisation of Escherichia coli isolates from the blood of haematological adult patients with bacteraemia: translocation from gut to blood requires the cooperation of multiple virulence factors. European Journal of Clinical Microbiology & Infectious Diseases, 2015. 34(6): p. 1135-1143.
[55] Tenover, F.C., et al., Characterization of nasal and blood culture isolates of methicillin-resistant Staphylococcus aureus from patients in United States hospitals. Antimicrobial agents and chemotherapy, 2012. 56(3): p. 1324-1330.
[56] Dimitrov, T., et al., Etiology and antibiotic susceptibility patterns of community-acquired urinary tract infections in a Kuwait hospital. Medical principles and Practice, 2004. 13(6): p. 334-339.
[57] Killgore, K.M., K.L. March, and B.J. Guglielmo, Risk factors for community-acquired ciprofloxacin-resistant Escherichia coli urinary tract infection. Annals of Pharmacotherapy, 2004. 38(7-8): p. 1148-1152.
[58] Kader, A.A. and A. Kumar, Prevalence and antimicrobial susceptibility of extended-spectrum β-lactamase-producing Escherichia coli and Klebsiella pneumoniae in a general hospital. Annals of Saudi medicine, 2005. 25(3): p. 239-242.
[59] Mansouri, S. and S. Shareifi, Antimicrobial resistance pattern of Escherichia coli causing urinary tract infections, and that of human fecal flora, in the southeast of Iran. Microbial Drug Resistance, 2002. 8(2): p. 123-128.
[60] Kehinde, E.O., et al., Bacteriology of urinary tract infection associated with indwelling J ureteral stents. Journal of endourology, 2004. 18(9): p. 891-896.
[61] Adembri, C., A. Novelli, and S. Nobili, Some Suggestions from PK/PD Principles to Contain Resistance in the Clinical Setting—Focus on ICU Patients and Gram-Negative Strains. Antibiotics, 2020. 9(10): p. 676.
[62] Qosimah, D., D.E. Aryani, and M.A.G. Beltran, Diabetes sepsis on Wistar rat strain (Rattus norvegicus) induced by streptozotocin and bacteria Staphylococcus aureus. Veterinary World, 2019. 12(6): p. 849.
[63] Gupta, K., D. Scholes, and W.E. Stamm, Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women. Jama, 1999. 281(8): p. 736-738.
[64] Dornbusch, K., A. King, and N. Legakis, Incidence of antibiotic resistance in blood and urine isolates from hospitalized patients. Report from a European collaborative study. Scandinavian journal of infectious diseases, 1998. 30(3): p. 281-288.