

Microorganisms Resistance Pattern and Antibiotic Prescriptions in Patients Admitted to the Intensive Care Unit in Ghazy AL Hariri Hospital

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Abstract

Introduction: Resistance to antibiotics has emerged recently due to the misuse of antibiotics and is a threat to the health-care system, especially in developing countries like Iraq where there are no antimicrobial stewardship programs in most intensive care units (ICU).

Materials and Method: This was an observational, cross-sectional study done in the ICU of Ghazi AL Hariri hospital, Medical City/Iraq. All patients getting admitted to ICU from both genders were included in the study. Samples taken for culture and sensitivity tests included blood, urine, tracheostomy tube, sputum, cerebrospinal fluid, central venous line, and bed sore swab.

Results: 43 patients satisfied the inclusion and exclusion criteria and were included in the study. The most common isolated pathogens were pseudomonas in sputum and blood samples, Acinetobacter in wounds and operation skin site infection, Klebsiella in central venous line, and bed sore swab, while Candida in the urine. Klebsiella was the most frequently isolated in overall culture results, it was most sensitive to imipenem, meropenem, and amikacin.

Conclusion: Ceftriaxone was the most commonly used antibiotic as an empiric treatment followed by meropenem and amikacin. Most of the isolated pathogens (> 90%) had resistance to ceftriaxone. ICU-acquired Klebsiella, P. aeruginosa, and Acinetobacter predominate hospital-acquired infections.

Keywords: Intensive care unit, Microorganisms resistance, Antibiotics.

Introduction

Infections are a common cause of hospital admission, and hospital-acquired infections are an increasingly common condition, mainly within the acute/critical care setting^[1]. Incidence of hospital-acquired infections in the Intensive Care Unit (ICU) has been stated to be about 2–5 times greater than in

the general inpatient hospital residents. These infections add considerable costs, morbidity, and mortality to the patients. The epidemiology, microbiology, and impact of ICU-acquired infections such as ventilator-associated pneumonia (VAP), catheter-associated urinary tract infections, and catheter-related bloodstream infections have been comprehensively studied and reported in the western literature^[2]. There is growing evidence to propose that rates of ICU-acquired infections might even be more significant in developing countries^[3]. ICU is a center for the development of antibiotic-resistant Gram-negative bacteria, and multi-resistant Gram-positive infections, since of high degrees of antibiotic usage, quick patient turnover, the immunological vulnerability of acutely ill patients, and recurrent interaction between healthcare staffs and patients, enabling cross-

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transmission. Antibiotic stewardship programs are considered essential to reduce antibiotic resistance^{[4],[5]}. There is inadequate literature concerning common ICU-acquired infections in the Iraqi setting, and therefore, western guidelines are deduced for the treatment of these infections. The local distinctions in the incidence, microbiology, and resistance patterns within Iraq are not well documented yet. Local guidelines for the prevention and treatment of these infections cannot be made without a proper assessment of the region-specific study. Hereafter, we sought to perform a cross-sectional, prospective data collection evaluating the microbiology, resistance patterns, and outcomes of ICU infections. Although the developments in modern medicine and intensive care, the rate of sepsis in intensive care units (ICUs) remains high. In a global study of 1265 ICUs, 60 % of ICU patients at the period of the study were considered infected, with infection found to be a strong independent predictor for mortality^[6]. The threats of infection in general and with a resistant pathogen in particular, increased with the interval of patient stay in the ICU. Several influences contribute to the elevated incidence of these infections in the ICU and the related poor patient outcomes, in comparison with patients in different hospital wards, patients in ICUs have more chronic comorbid diseases and more acute physiologic instabilities and thus are relatively immunosuppressed^[7].

Materials and Method

This was a hospital-based observational, cross-sectional study done in the intensive care unit (ICU) of Ghazi AL Hariri hospital, Medical city/Baghdad, Iraq during the period from 1st October 2018 to the 1st August 2019. All patients getting admitted to ICU from both genders with different infections will include in the study. Demographic details, comorbidities, duration of ICU admission, number of antibiotics used, antibiotic prescription, antimicrobial resistance pattern of patients will be collected. Patients who are HIV positive, who could not provide an adequate specimen, and patients who died within 48 h after admission, patient with incomplete data. Since most of the patients were incapable of talking, because of being critically ill or intubated (by endotracheal tube or tracheostomy), data collection mainly from patients' case files and unit's staff (doctors, nurses, pharmacists, and lab technicians). Samples taken for culture and sensitivity tests included blood, urine, tracheostomy tube, sputum, cerebrospinal fluid, central venous line, and bedsore swab.

Statistical Analysis: Data of 43 cases and 430 samples collected from the admitted patients analyzed by using the statistical package for social sciences (SPSS) software version 23, IBM, Chicago, US, for windows. Descriptive statistics presented as mean, frequencies, and proportion (%). Finally, results are presented in tables and or figures with an explanatory paragraph.

Results

Throughout the study period, 105 patients admitted to ICU were enrolled, 62 of them excluded from the study, 43 patients satisfied inclusion and exclusion criteria, and included in the study. The mean age of the study population was 50.72 ± 20.73 and of whom 23 (52.30%) were men, and 20 (46.5 %) were females. From the 43 participants 23 (53.5%) survived and 20 (46.5 %) died. The most common admitted cases to the ICU was stroke representing (20.9% [9/43]), postoperative cases (18.6% [8/43]). The duration of hospitalization was between 2 – 180 days. The mean duration of admission was 22.38 (SD ± 15.4) days. The outcome of the admitted patients was as follows: 20 patients went back to their original wards to finalized their therapies, three patients discharged home. Twenty patients died (mortality rate of 46.5%). All patients received pharmacological treatments regarding their conditions, involving empirical antibiotics depending on the physician's opinion about the clinical state of the patient. The mean period for empiric treatment was 5.67 (SD ± 4.92) days, the empirical antibiotics used in variable combinations considering the patient's condition; ceftriaxone was the most commonly used antibiotic as an empiric treatment (39.7%) followed by meropenem (23.5%) and amikacin (5.9%) (Table 1).

Table 1: Antibiotics used for empiric treatment.

Antibiotic	Frequency	Percent
Ceftriaxone	27	39.7
Meropenem	16	23.5
Amikacin	4	5.9
Piperacillin/Tazobactam	3	4.4
Levofloxacin	3	4.4
Metronidazole	3	4.4
Ciprofloxacin	2	2.9
Imipenem	2	2.9
Vancomycin	2	2.9
Amoxicillin	2	2.9

Antibiotic	Frequency	Percent
Amoxicillin/Clavulanic acid	1	1.5
Ceftazidem	1	1.5
Azithromycin	1	1.5
Linezolid	1	1.5
Total	68	100.0

The antibiotics, as mentioned earlier used as a single agent or in combinations of two or three agents according to the patient’s status, 48.8% of the patients given a combination of two or more antibiotics. All

patients underwent culture and sensitivity (CS) test as soon as they were admitted to the ICU, the meantime needed for CS test results to return to the ICU was 10 (SD± 5.1) days, range (2 – 25) days. In most of the cases, the antibiotics changed according to the results of the bacteriological test. Samples obtained for CS tests included blood, sputum, urine, tracheostomy tube, central venous line, foley catheter tip, and bedsores. The number of positive cultures and sensitivity test results obtained in 327 samples out of a total of 430 tests. The most common isolated pathogen was summarized in Figure (1).

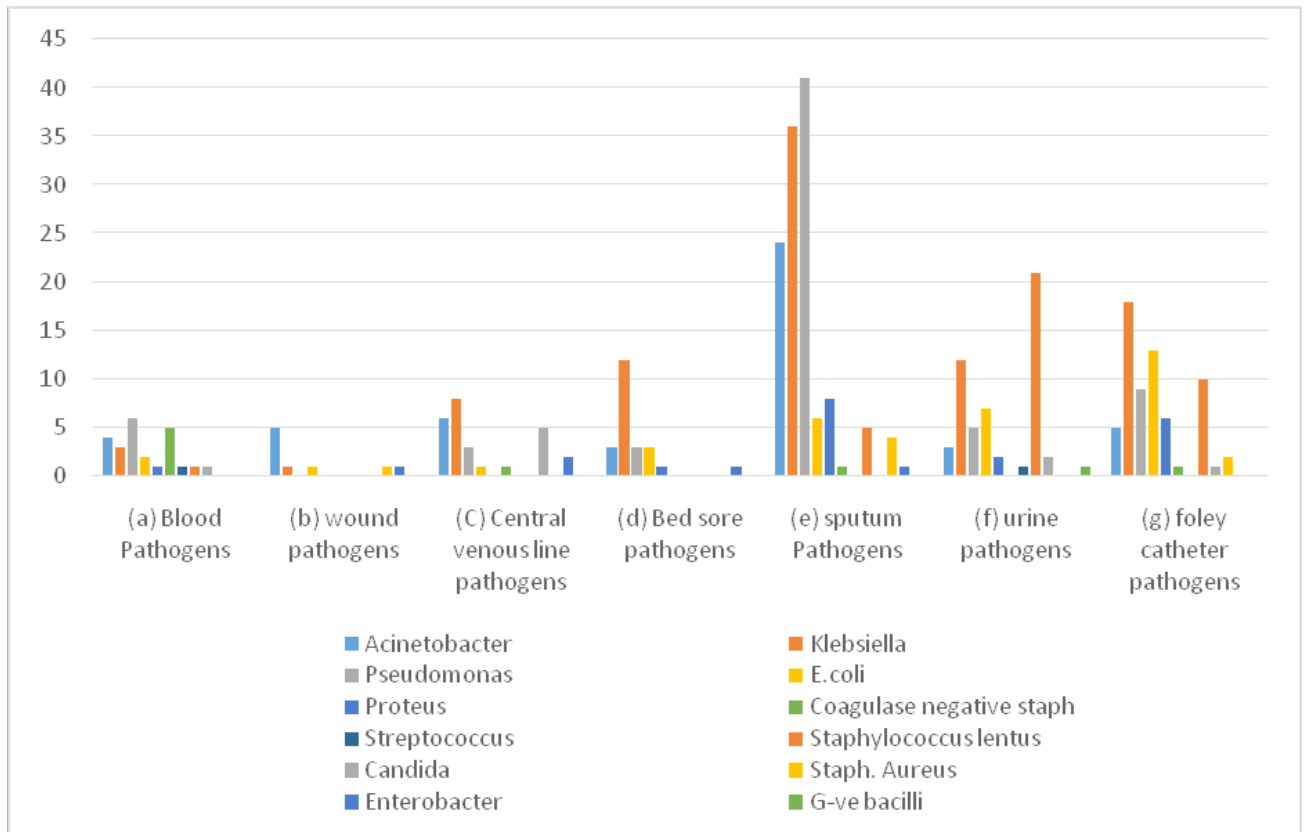


Figure 1: (a) blood cultures pathogens (b) wound swab pathogens (c) central venous line pathogens (d) bedsore pathogens(e) sputum cultures pathogens (f) urine cultures pathogens (g) Foley catheter cultures pathogens.

In overall culture results in a total of 327 tests the most frequently isolated pathogens were Klebsiella 27.5% (90/327), followed by Pseudomonas 20.5% (67/327) and Acinetobacter 15.3% (50/327) Table (2).

Table 2: The frequency and percentage of isolated pathogens in cultures and sensitivity tests

Pathogens		Frequency	Percent
Valid	Klebsiella	90	27.5
	Pseudomonas	67	20.5
	Acinetobacter	50	15.3
	Candida	42	12.8
	E.coli	33	10.1
	Proteus	18	5.5
	Enterobacter	10	3.1
	Coagulase -ve staphylococcus	7	2.1
	Staphylococcus aureus	5	1.5
	Streptococcus	2	.6
	Gram -ve bacilli	1	.3
	Burkholderiacepacia	1	.3
	Total	327	100.0

These microorganisms tested for their sensitivity to several antimicrobial kits to about 30 antibiotics. From the results of Klebsiella sensitivity tests, there are only 188 time-sensitive results of the tested antibiotics (about

30) for a total of 90 times detected positive culture tests. Klebsiella Pneumonia was most commonly sensitive to imipenem 55% (50/90), followed by meropenem 30% (27/90), and amikacin 26.6% (24/90) Figure (2).

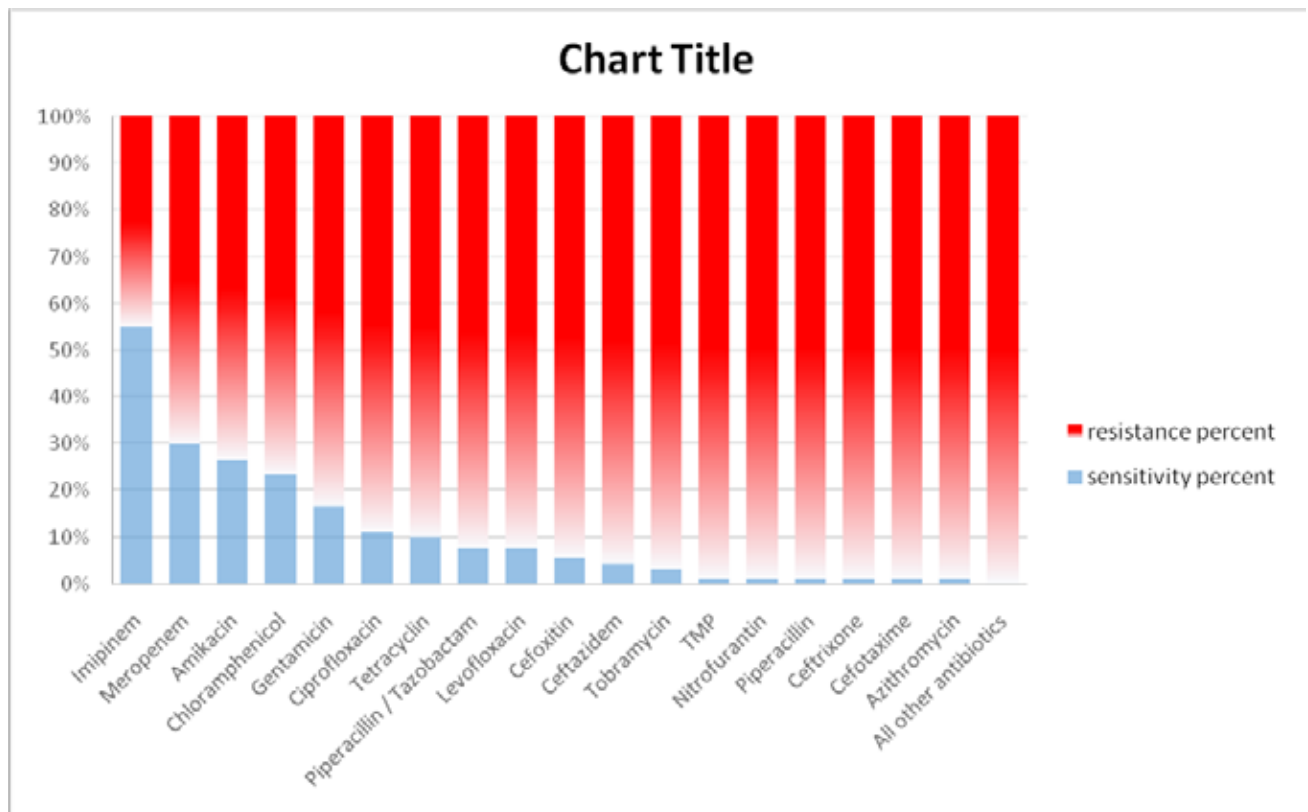


Figure (2): Percent of Klebsiella pneumonia sensitivity and resistance to antibiotics

In regards to *Pseudomonas* which they reported positively in 67 tests, it showed sensitivity to piperacillin/tazobactam in 43.2%, imipenem 35.5%, ceftazidime 31.3% Figure (3).

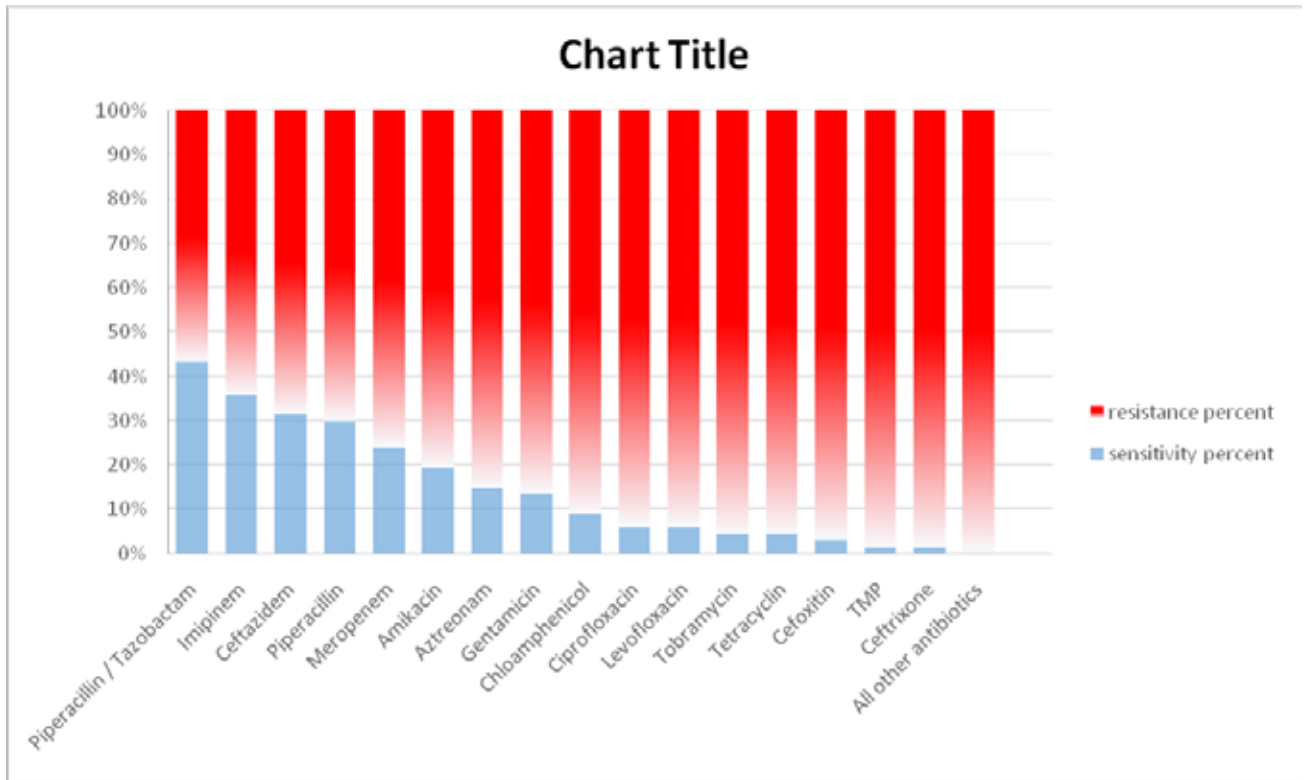


Figure (3): Percent of *Pseudomonas aeruginosa* sensitivity and resistance to antibiotics

Acinetobacter baumannii which was isolated in 15.5% of all positive results showed sensitivity to amikacin in 22%, tetracyclin in 18%, ampicillin, gentamicin, tobramycin, imipenem were 14% for each one, Figure (4).

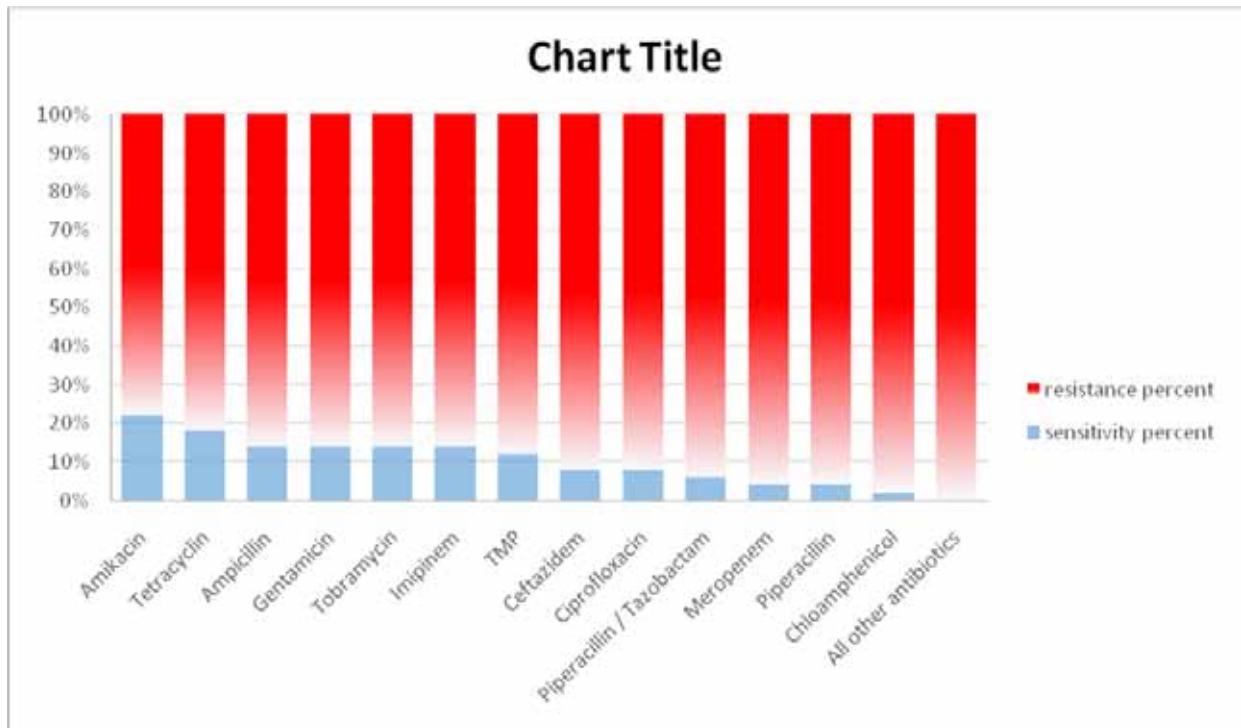


Figure (4): Percent of *Acinetobacter baumannii* sensitivity and resistance to antibiotics

Proteus showed sensitivity in to piperacillin/tazobactam 61.1%, imipinem 55.5%, ciprofloxacin 44.4%, meropenem 44.4%, amikacin 38.8%, ceftazidem 33.3%, gentamicin 33.3%, cefoxitin 22.2%, cefotaxime 22.2%, chloamphenicol 16.6%, ceftriaxone 16.6%, aztreonam 11.1%, amoxicillin/clavulanic acid 11.1%, TMP 11.1%, piperacillin 5.5%, and levofloxacin 5.5%.

E. coli was sensitive to imipenem in 60.6%, chloramphenicol 36.6%, and 33.3% sensitive to meropenem, amikacin 30.3%, ciprofloxacin 21.2%, Piperacillin/Tazobactam 21.2%, gentamicin 18.1%, nitrofurantoin 18.1%, levofloxacin 9%, tetracyclin 9%, ceftazidem 6%, cefoxitin 6%, ampicillin, aztreonam, tobramycin, ceftriaxone and cefotaxime 3%. *Streptococcus pneumoniae* was sensitive only in two times,

once for tetracycline and the second for trimethoprim-sulfamethoxazole. *Enterobacter* was sensitive for chloramphenicol in 40%, Ciprofloxacin in 30%, Imipenem in 20%, and 10% for each aztreonam, levofloxacin, tetracycline. *Staphylococcus aureus* was sensitive to chloramphenicol in 50%, 30% to vancomycin, and 20% to trimethoprim-sulfamethoxazole. Coagulase-negative staphylococcus was 100% sensitive to Vancomycin, tetracyclin in 42%, gentamicin & nitrofurantoin in 28%, and chloramphenicol 14%. *Candida Albicans* was the most isolated fungi it was sensitive 6 times to miconazole, 5 times for both fluconazole and ketoconazole. *Staphylococcus lentus* isolated in one case of sepsis. Overall bacterial sensitivity between the tested antibiotics showed 17.7% to imipenem, amikacin, and meropenem 10.2%. Table (3).

Table (3): Overall bacterial sensitivity to antibiotics in the 327 positive culture tests

Tested Antibiotics		Frequency	Percent
Valid	Imipinem	113	34.5
	Amikacin	65	19.8
	Meropenem	65	19.8
	Piperacillin/Tazobactam	57	17.4
	Chloramphenicol	53	16.2
	Gentamicin	45	13.7
	Ceftazidem	38	11.6
	Ciprofloxacin	36	11
	Tetracyclin	29	8
	Piperacillin	24	7.3
	Levofloxacin	16	4.8
	Aztreonam	14	4.2
	TMP	14	4.2
	Tobramycin	14	4.2
	Cefoxitin	13	3.9
	Vancomycin	10	3
	Nitrofurantoin	9	2.7
	Ampicillin	8	2.4
	Ceftriaxone	7	2.1
	Cefotaxime	6	1.8
Amoxicillin/Clavulanic acid	2	0.6	
Azithromycin	1	0.3	

Also, there are samples taken as a swab from the beds, ventilator machines, oxygen suppliers, fluid stands, floors, walls. coagulase-negative staphylococcus was the most frequently isolated pathogen followed by bacillus species.

Discussion

In the current study each patient with a documented or a suspected source of infection received antibiotic prescription by the physician in charge, and generally, it is grounded on a clinical basis and experience. And this is what followed in five tertiary care hospitals in Germany as mentioned by Wilke M et al. who stated that therapy grounded on local experiences might be appropriate for patients with low complicated pathogen risk score (CPRS) but insufficient for those with high CPRS^[8]. As well, in the current study, the meantime for culture and sensitivity results to come back to ICU was very long, this is a time-consuming step. This issue is also a challenge in therapeutic practice even in European countries. As there is a profound difference between countries in retrieving the results of the culture tests, for example in the United Kingdom, 2 hours are needed from collection to incubation while in Germany 20 hours are necessary for incubating the bacteria due to distant laboratories^[9], still, these times are much shorter than that in the settings followed in Ghazi Al Hariri center. Many studies are debating new method to reduce the period of detecting the causal organisms in the patients to enhance the choice of the antibiotics as early as possible and consequently improve the outcome. Such as a study that employed a new spectrometry method that provides rapid pathogen identification in critically ill patients with the capability to rule out infection within 6 hours. This has potential clinical and economic benefits^[10]. In the present study, the most frequently isolated pathogen was *Klebsiella pneumoniae*, and the lowest isolation rate was for *Burkholderiacepacia* and Gram-negative bacilli. Causative organisms diverge in different geographical areas. This result is differing from that previously published in Asian countries, a study conducted in a tertiary teaching hospital of Eastern India intensive care unit which stated *Pseudomonas* is the most isolated microorganism while the lower isolation rate was for the eCoagulase-negative staphylococci, *Enterobacter* spp, *Stenotrophomonas* spp, *Burkholderiacepacia*^[11]. In a study of Ghanshani et al. they found a higher rate of bacterial isolation for the following pathogens: *Acinetobacter*, *Klebsiella*, *Streptococcus*, *Pseudomonas*, and *Staphylococcus* ^[12]. Several studies from other

Asian countries such as Indonesia, Thailand stated that frequency of *Pseudomonas* isolation was about (26%–50%) followed by *Klebsiella* and *S. epidermidis* ^[13,14]. In another study, done in Turkey showed that *Pseudomonas* spp. were the most frequently isolated Gram-negative spp., followed by *Klebsiella* spp. *E. coli*, *Acinetobacter* spp. And *Enterobacter* spp. were the other commonly isolated organisms^[15]. Antimicrobial resistance is a major worldwide problem in ICU, including Iraq. ICUs are the main foci of antibiotic resistance within the hospital wards^[16]. Antimicrobial resistance is emerging due to the deficiency of hospital hygiene and the misuse of antibiotics^[17]. Antibiotic prescription in an ICU is mostly empirical and centered on previous practices; hereafter, patients who got improper empirical antibiotic treatments significantly increase hospital stay and increases mortality^[18] hospital-acquired infections originating from drug-resistant microorganisms further add to the existing problem. A striking outcome from this study was the degree of drug resistance among key pathogens. This study detected high drug resistance of *Klebsiella* to a commonly prescribed drug compared to a study done by Kumari et al.^[19], who observed similar levels. *P. aeruginosa* isolates showed a high rate of resistance to ceftriaxone, TMP, ciprofloxacin, levofloxacin, gentamicin, amikacin, the most effective antibiotics were piperacillin/tazobactam, imipenem, and ceftazidime. The similar result reported previously in a study by Radji et al.^[20] in which they stated *P. aeruginosa* isolates displayed a high rate of resistance to cefotaxime, cephalexin, and ceftriaxone. But in this study, amikacin was the most effective antibiotic, followed by imipenem, and meropenem. *Acinetobacter baumannii* is extremely resistant to antibiotics^[21]. In this study, the resistance was higher in *Acinetobacter* than all of the other isolated pathogens. This is in concordance to what was reported by Tran et al. where they stated that *Acinetobacter* was resistant to nearly all antibiotics. *Staphylococcus lentus* a zoonosis pathogen was reported for the first time as a cause of septic shock during the work on this research^[22]. *Proteus mirabilis* showed marked resistance to commonly used antibiotics. In the European and North American Surveillance study by Mark et al.^[23] they reported the resistance profile of *Proteus* in the US, Canada, Italy, Germany, and France. The resistance rate was different from ours; ceftriaxone resistance was (0.3%, 0%, 13.8%, 0%, 0%) in the US, Canada, Italy, Germany, and France respectively. On the other hand, *E. coli* showed high resistance to several broad-spectrum antibiotics, Best sensitivity results achieved by imipenem,

chloramphenicol, and meropenem. In comparison to what reported previously in a study by Zhanel et al.^[24], *E. coli* showed no resistance to amikacin, meropenem, and tigecycline. In the current study, ceftriaxone was the main antibiotic used as an empiric treatment followed by meropenem, amikacin, and piperacillin/tazobactam. This may be due to the previous experience with these drugs, its availability, its opened dispense with no limitation, and its broad spectrum of action. The infrequent use of chloramphenicol may explain its probable activity against isolated pathogens as shown by culture studies, and this, in turn, should alert the clinicians in charge (physician and the clinical pharmacists) to review their choices of the empirical therapy medications and to reduce their use of ceftriaxone as first choice antibiotic in the empirical management. Source of infections seem to be from the ICU equipment like the ventilator, sucker, fluid stands, and oxygen suppliers. Also, the wall, floor, and patients bed showed colonization with different microorganisms; Coagulase –ve staphylococcus and *Bacillus* spp were the most predominant pathogens. This is the leading cause of secondary endogenous infections and exogenous infection. It accounts for more than one-third of all types of ICU infections according to what reported in a study by Mukhopadhyay^[25]. Ceftriaxone resistance was noted by Tran et al. who studied the resistance of bacteria in ICU against several antimicrobials and showed that most of *Acinetobacter*, *Klebsiella*, and *Pseudomonas* were resistant to ceftriaxone.

Conclusion

This study concluded that ICU-acquired *Klebsiella*, *P. aeruginosa*, and *Acinetobacter* predominate hospital-acquired infections. More disturbingly, all of them were multiple-drug resistant. The result here supports the view that multidrug resistance is a global public health threat, and highlights the need to study combined therapies and rational treatment strategies. Ceftriaxone was the most common empirical antimicrobial prescribed to patients admitted to ICU. Most of the isolated pathogens (> 90%) had resistance to it. Suitable antibiotic employment in ICU is crucial not only in guaranteeing the best outcome but also in inhibiting the development of multidrug-resistant bacteria.

Ethical Approval: The study protocol approved by the Scientific Council of the Iraqi Board of Medical Specialization.

Conflict of Interest: Nil

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