

## Trend of Antibiotics Usage in the Intensive Care Unit in the Medical City in Baghdad

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### Abstract

High frequencies of multidrug resistant organisms were observed worldwide in intensive care units which is a warning as to use the only few effective antimicrobials wisely to reduce selective pressure on sensitive strains.

The aim of the current study is to assess the compliance of the currently followed antibiotic prescribing pattern in the intensive care unit in an Iraqi hospital with the international guidelines. A cross-sectional study was done in the intensive care unit (ICU) of the Surgical Specialties Hospital, Medical City in Baghdad from the 30<sup>th</sup> of November 2011 to the 5<sup>th</sup> of May 2012. Patients were followed until they were discharged or died to see any change in condition, response to drugs, devices used, and medications.

During the period of the study, there were 46 patients admitted to the ICU of whom 23 (50%) were males and 23 (50%) were females. The age range of patients was between 16 and 85 years. The mean of age of patients was 44.52 (SD±18.45) years. All patients underwent culture and sensitivity test as soon as they were admitted to the ICU, but out of 46 patients only 16 (34.78%) of them have culture and sensitivity tests results retrieved. The number of patients, in whom the antibiotics were prescribed or changed according to culture and sensitivity tests, was six patients only (13.04%). Ceftriaxone was the most commonly used antibiotic as an empiric treatment followed by ampicillin-cloxacillin combination and meropenem, while clarithromycin and ciprofloxacin were among the least used. The bacterial culture and sensitivity tests of different samples obtained from the patients showed that the most effective antibiotic was tobramycin (90%) followed by ciprofloxacin and levofloxacin (69.2%) for each and the least effective (bacterial resistance) was ceftriaxone (33.3%) and cefotaxime (28.5) among others.

In conclusion, there is a critical need for reviewing the trend of antibiotic use in the ICUs depending more on lab. tests to identify the most effective drugs and to minimize the emergence of resistant infection.

**Keywords:** ICU, Antibiotic resistance, Culture and sensitivity tests.

### طريقة استخدام المضادات الحيوية في وحدة العناية المركزة في مدينة الطب في بغداد زينة مظفر النعمة<sup>\*1</sup>

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### الخلاصة

نظرا لكثرة وجود الكائنات المقاومة للعديد من الادوية في وحدات العناية المركزة، لابد من التوجه لاستخدام المضادات الحيوية بحكمة للتقليل من الضغط على السلالات الحساسة. الهدف من الدراسة الحالية هو لتقييم امثال الوصفات الطبية للمضادات الحيوية المتبعة حاليا في وحدة العناية المركزة في مستشفى عراقي مع الوصفات المتبعة دوليا. الدراسة الحالية مقطعية اجريت في وحدة العناية المركزة في مستشفى الجراحات التخصصية في مدينة الطب في بغداد من 30 تشرين الثاني 2011 إلى 5 ايار 2012. تم متابعة المرضى الداخلين للوحدة حتى خروجهم أو موتهم لمعرفة أي تغيير في الحالة والاستجابة للأدوية وكذلك الأجهزة المستخدمة والادوية المستخدمة.

خلال فترة الدراسة، كان هناك 46 مريضا ادخل الى وحدة العناية المركزة منهم 23 (50%) من الذكور و 23 (50%) من الاناث ذوي الفئة العمرية من 16 إلى 85 عام وكان متوسط عمر المرضى 44,52 (الانحراف المعياري ±18,45) عام. خضع جميع المرضى عند الدخول لردهة العناية المركزة لاختبارات الحساسية للمضادات الحيوية، ولكن تم الحصول على نتائج الاختبارات ل 16 (34,78) مريض فقط من 46 مريض، وكان عدد المرضى الذين تم وصف او تغيير المضادات الحيوية اعتمادا على نتائج اختبارات الحساسية 6 (13,04%) فقط. واطهرت الدراسة ان دواء سفترايكسون الاكثر شيوعا في الاستخدام كعلاج اولي ثم يليه الدواء المركب من الاميسيلين والكلوكساسولين ثم دواء الایمیبیبینیم. وكانت الادوية التالية كلاريثروميسين و سيبروفلوكساسين الاقل استخداما. ووضحت نتائج اختبارات الحساسية التي تم الحصول عليها في الدراسة الحالية ان المضاد الحيوي الاكثر فعالية هو توبراميسين (90%) و يليه بالفعالية دواء سيبروفلوكساسين و الليفولوكساسين (69,2%) لكل منهما و الاقل فعالية في مقاومة البكتريا هو سفترايكسون (33,3%) و الليفولوكساسين (28,5%).

في الختام لابد من التنويه الى ان هناك حاجة ماسة لاعادة النظر في طريقة استخدام المضادات الحيوية في وحدات العناية المركزة والاعتماد على التحليلات المخبرية لتحديد الدواء الاكثر فاعلية للتقليل من العدوى المقاومة للادوية. الكلمات المفتاحية: وحدة العناية المركزة، مقاومة المضادات الحيوية، اختبارات الحساسية.

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## Introduction

Intensive care units (ICU) are epicenters for the emergence of antibiotic-resistant Gram-negative bacteria<sup>(1,2)</sup>, and multi-resistant Gram-positive infections, largely due to the inappropriate use of antimicrobials<sup>(3)</sup>.

In addition to that, rapid patient turnover, immunological susceptibility of acutely ill patients, and frequent contact between healthcare workers and patients, facilitate cross-transmission. Antibiotic stewardship programs are considered important to reduce antibiotic resistance, but the effectiveness of strategies such as, for instance, antibiotic rotation, have not been determined rigorously<sup>(1)</sup>.

The patterns of such resistance clearly vary among hospitals. Inadequate empirical antimicrobial treatment has also resulted in greater patient morbidity, higher mortality rates, and increased healthcare costs<sup>(4)</sup>.

High frequencies of multidrug resistant organisms were observed in intensive care units which is a warning as to use the only few effective antimicrobials wisely to reduce selective pressure on sensitive strains<sup>(5)</sup>.

Hospital-acquired pneumonia often occurs as ventilator-associated pneumonia is the most frequent hospital infection in ICUs. Early adequate antimicrobial therapy is an essential determinant of clinical outcome, its diagnosis and management are complex. Consequently, its prevention becomes a cornerstone in daily clinical practice<sup>(6,7)</sup>.

Inadequately treated patients had a higher complicated pathogen risk score (CPRS) compared to those who received adequate therapy. This shows that therapy based on local experiences may be sufficient for patients with low CPRS but inadequate for those with high CPRS<sup>(7)</sup>.

Therefore, guideline-adherent initial intravenous antibiotic therapy is clinically superior, saves lives and is less expensive than non-guideline adherent therapy. Using a CPRS can be a useful tool to determine the right choice of initial intravenous antibiotic therapy<sup>(7)</sup>.

The aim of the current study is to assess the compliance of the currently followed antibiotic prescribing pattern in the intensive care unit in Iraqi hospitals with the international guidelines.

## Methods

A cross-sectional study was done in the intensive care unit (ICU) of the Surgical Specialties Hospital, Medical City in Bagdad from the 30<sup>th</sup> of November 2011 to the 5<sup>th</sup> of May 2012.

The ICU of the specialty hospital had 16 beds with 2 isolated rooms each containing 1 bed, there is also a side lab for simple and emergency investigations. The ICU receives either postoperative patients mainly neurosurgery or severely injured patients and sometimes medical patients with neurological diseases. Admission is usually the responsibility of the senior physician of the ICU. The staff of the ICU consists of seniors specialist in anesthesia and intensive care and senior residents with trained nursing staff. Clinical pharmacist is also a part of the medical team.

Since most of the patients were unable to talk normally, because of being critically ill or intubated (by endotracheal tube or tracheostomy), data were taken mainly from case sheets of patients and from medical staff (doctors, nurses, pharmacists, and lab technicians) samples taken for culture and sensitivity tests included urine, tracheostomy tube, blood, sputum, cerebrospinal fluid, and ventriculo-peritoneal shunt. Culture and sensitivity tests were done using Kirby Bauer disk diffusion method<sup>(8)</sup>.

Patients were followed until they were discharged or died to see any change in condition, response to drugs, devices used, medications (duration of treatment, route of administration, dosage, side effects, and frequency).

Children were excluded because the study was designed for adults only.

The followings were reported for each patient: Systemic disease, diagnosis, devices used, causes of each admission, culture results, antibiotic(s) used, and indication for each and the outcome of the patient (discharged or died).

Chi square was used to calculate the differences between groups using *P* value below 0.05 as significant.

## Results

During the period of the study, there were 46 patients admitted to the ICU of whom 23 (50%) were males and 23 (50%) were females.

The age range of patients was between 16 and 85 years. The mean of age of patients was 44.52 (SD ±18.45) years.

The duration of admission to ICU ranged from one to 142 days. The mean of duration of admission was 27.45 (SD ±32.2) days.

The fate of the patients who were admitted to ICU during the period of study was as follows: 23 patients returned back to their original wards to complete their therapy, 22 patients died (mortality rate 47.8%) and one patient was transferred outside Iraq to complete his treatment.

All patients were receiving medical treatment according to their condition including empirical antibiotics depending on the clinical state of the patient and the experience of the physician.

All patients underwent culture and sensitivity test as soon as they were admitted to the ICU, but out of 46 patients only 16 (34.78%) of them have culture and sensitivity tests results retrieved and the total number of tests performed for these 16 patients was 25 tests and as follows: urine: five culture and sensitivity tests, blood: seven culture and sensitivity tests, sputum: three culture and sensitivity tests, tracheostomy swab: eight culture and sensitivity tests, cerebrospinal fluid: one and ventriculoperitoneal shunt swab: one test.

The mean time needed for culture and sensitivity test results to return back to the ICU was 9.58 (SD± 4.66) days, range (1-27 days).

The number of patients, in whom the antibiotics were prescribed or changed according to culture and sensitivity tests, was six (13.04%) patients only.

The mean duration for empiric treatment was 5.32 (SD ±5.37) days, the empirical antibiotics were used in different combinations according to the condition of the patient and the experience of the physician, ceftriaxone was the most commonly used antibiotic as an empiric treatment (35.5%) followed by ampicillin–cloxacillin combination (6.6%) and meropenem (4.4%), while clarithromycin, and ciprofloxacin were among the least used (2.2%) for each (Table 1).

**Table (1): Antibiotics used for empiric treatment.**

	Antibiotic (S)	Number of patients	Percentage of patients (%)
1	Ceftriaxone	16	35.5
2	Ceftriaxone + metronidazole.	3	6.6
3	Ceftriaxone + ampiclox*.	3	6.6
4	Ceftriaxone + ampiclox + metronidazole.	3	6.6
5	Meropenem.	2	4.4
6	Meropenem + ceftriaxone	2	4.4
7	Meropenem + metronidazole	1	2.2
8	Meropenem + azithromycin	1	2.2
9	Meropenem + vancomycin	1	2.2
10	Meropenem + clarithromycin + ciprofloxacin	1	2.2
11	Ceftriaxone + vancomycin	1	2.2
12	Ceftriaxone + ciprofloxacin	1	2.2
13	Ceftriaxone + amikacin	1	2.2
14	Ceftriaxone + amikacin + ampiclox	1	2.2
15	Ceftriaxone + azithromycin	1	2.2
16	Ceftazidime	1	2.2
17	Ceftazidime + ampiclox	1	2.2
18	Ceftazidime + metronidazole	1	2.2
19	Ceftazidime + teicoplanin	1	2.2
20	Azithromycin	1	2.2
21	Vancomycin + metronidazole + cefotaxime	1	2.2
22	Cefotaxime + metronidazole +ampiclox +ceftriaxone	1	2.2

\*ampiclox: ampicillin-cloxacillin combination.

Postoperative patients represented the majority of the patients admitted to the ICU, they were 21 out of 46 patients, followed by patients with motor neuropathy 7 out of 46 patients, (Table 2).

Types of bacteria isolated from the patients were as follows: out of 16 who have culture test, results of 8 cultures show no growth of bacteria, 7 cultures with one species of bacteria, and 6 cultures with two species of bacteria, (Table 3).

Samples taken for culture and sensitivity tests included urine, tracheostomy tube, blood, sputum, cerebrospinal fluid, and ventriculoperitoneal shunt swab, and many bacteria were isolated, and the sensitive or resistant antibiotics were displayed in details in table 4.

Table (2): Diseases of patients admitted to ICU.

	Disease	No. of patients
1	Postoperative neurological surgery	14
2	Postoperative non-neurological surgery	7
3	Motor neuropathy	7
4	CVA	5
5	Unknown diagnosis	1
6	RTA	2
7	Miscellaneous	10
	Pulmonary fibrosis	1
	Acute pancreatitis	1
	Lung cancer metastasis	1
	Kyphosis	1
	Head trauma	1
	Burn	1
	Acute respiratory distress	2
	Severe chest infection	1
	Hypovolemic shock	1
	Total	46

Table (3): Types and frequency of bacteria isolated from patients of the ICU.

Type of bacteria isolated from patients	Frequency of bacteria isolated from patients*	Percentage of bacteria isolated from patients
<i>Klebsiella</i> spp.	7	53.8
<i>Acinetobacter</i> spp.	5	38.46
<i>Pseudomonas</i> spp.	3	23.07
<i>Baurkholderia</i> spp.	2	15.3
<i>Proteus</i> spp.	1	7.6
<i>Coagulase</i> -ve <i>staphylococci</i>	1	7.6

\*Six patients have two species of bacteria.

Table (4): Causative bacteria isolated from patients and their sensitivity to antibiotics in each sample in the ICU

	Sample	Causative organism	Sensitive antibiotic(s)	Resistant antibiotic(s)
1	Urine	<i>Klebsiella</i> spp.	Amikacin, Nitrofurantoin.	Ceftazidime, cefalothin, cefotaxime, ceftriaxone, co-trimoxazole, cefotetan, ceftioxin, ciprofloxacin, levofloxacin, gentamicin, tobramycin, tetracycline, chloramphenicol, piperacillin.
		<i>Klebsiella</i> spp.	Co- trimoxazole.	Amikacin, aztreonam, ceftazidime, cefalothin, cefotetan, ceftioxin, ciprofloxacin, levofloxacin, gentamicin, tobramycin, tetracycline, chloramphenicol, Nitrofurantoin.
		<i>Acinetobacter</i> spp.	Tetracycline, gentamicin, tobramycin.	Amikacin, ampicillin, aztreonam, amoxiclav*, ceftazidime, cefuroxime, cefalothin, co-trimoxazole, nitrofurantoin, ceftriaxone, cefixime.
2	Tracheostomy swab	<i>Acinetobacter</i> spp.	Tetracycline, doxycycline, minocycline.	Amikacin, ceftazidime, cefotaxime, ceftriaxone, gentamicin.
		<i>Baurkholderia</i> spp.	Co- trimoxazole.	Ceftazidime.
		<i>Pseudomonas</i> spp.	Amikacin, ceftazidime, ciprofloxacin, levofloxacin, gentamicin, tobramycin.	Piperacillin.
		<i>Acinetobacter</i> spp.	Amikacin, aztreonam, ceftazidime, cefotaxime, ceftriaxone, ciprofloxacin, levofloxacin, gentamicin, tobramycin, tetracycline.	Piperacillin.
		<i>Pseudomonas</i> spp.	Amikacin, ciprofloxacin, levofloxacin, gentamicin, tobramycin.	Piperacillin.

**Table (4): (Continued) causative bacteria isolated from patients and their sensitivity to antibiotics in each sample in the ICU**

	Sample	Causative organism	Sensitive antibiotic(s)	Resistant antibiotic(s)
		<i>Pseudomonas</i> spp.	Amikacin, ceftazidime, ciprofloxacin, levofloxacin, gentamicin, tobramycin.	Piperacillin.
		<i>Proteus</i> spp.	Amikacin, cefotaxime, ceftriaxone, cefotetan, ceftazidime, ciprofloxacin, levofloxacin, tobramycin.	Ceftazidime, piperacillin, tetracycline, chloramphenicol.
		<i>Acinetobacter</i> spp.	Nil	
3	Sputum	<i>Baurkholderia</i> spp.	Co- trimoxazole.	Ceftazidime.
		<i>Klebsiella</i> spp.	Cefotetan, ceftazidime, ciprofloxacin, levofloxacin, gentamicin, tobramycin, tetracycline, chloramphenicol.	Piperacillin.
		<i>Acinetobacter</i> spp.	Cefotetan, ceftazidime, ciprofloxacin, levofloxacin, gentamicin, tobramycin, chloramphenicol.	Tetracycline.
4	Blood	<i>Klebsiella</i> spp.	Tetracycline.	Amikacin, aztreonam, ceftazidime, cefotaxime, ceftriaxone, cefotetan, ceftazidime, ciprofloxacin, levofloxacin, gentamicin.
		<i>Coagulase –ve staphylococci</i>	Tetracycline, doxycycline, vancomycin.	co-trimoxazole, clarithromycin, erythromycin, aztreonam, ciprofloxacin, levofloxacin, gentamicin, chloramphenicol, penicillin, clindamycin, methicillin.
		<i>Klebsiella</i> spp.	Ciprofloxacin, levofloxacin	Piperacillin.
5	CSF**	<i>Klebsiella</i> spp.	Amikacin, cefotetan, ceftazidime, ciprofloxacin, levofloxacin, gentamicin, tobramycin, tetracycline, chloramphenicol.	Ceftazidime, cefotaxime, ceftriaxone, piperacillin.
6	VP*** shunt swab	<i>Klebsiella</i> spp.	Amikacin, cefotetan, ceftazidime, ciprofloxacin, levofloxacin, gentamicin, tobramycin, tetracycline, chloramphenicol.	Aztreonam, ceftazidime, cefotaxime, ceftriaxone, piperacillin.

\*Amoxiclav: amoxicillin clavulanic acid combination. \*\*CSF: Cerebrospinal fluid.

\*\*\*VP shunt: Ventriculoperitoneal shunt.

The bacterial culture and sensitivity tests of different samples obtained from the patients showed that tobramycin has the greatest sensitivity (90%) while the resistance was low (10%) and this difference is significant ( $P$  value=0.0003), whereas ceftriaxone sensitivity

was low (33.3%) and the resistance was high (66.7%) and this is a non significant difference ( $P$  value= 0.248). Ciprofloxacin and levofloxacin were the second effective antibiotics with high sensitivity (69.2%), (Table 5).

Table (5): Results of culture and sensitivity tests\*

	Antibiotic	Number of sensitive results (%)	Number of resistant results (%)	Total sensitivity tests	P value
1	Doxycycline	2(100)**	0(0)	2	0.04(S)
2	Minocycline	1(100)**	0(0)	1	0.157(NS)
3	Vancomycin	1(100)**	0(0)	1	0.157(NS)
4	Tobramycin	9(90)	1(10)	10	0.0003(S)
5	Ciprofloxacin	9 (69.2)	4 (30.8)	13	0.049(S)
6	Levofloxacin	9 (69.2)	4 (30.8)	13	0.049(S)
7	Amikacin	8(66.6)	4(33.4)	12	0.102(NS)
8	Tetracycline	7(63.6)	4(36.4)	11	0.200(NS)
9	Gentamicin	8(61.5)	5(38.5)	13	0.239(NS)
10	Cefoxitin	4(57.1)	3(42.9)	7	0.592(NS)
11	Cefotetan	3(50)	3(50)	6	1(NS)
12	Co-trimoxazole	3(42.8)	4(57.2)	7	0.592(NS)
13	Nitrofurantoin	1(33.3)	2(66.7)	3	0.414(NS)
14	Ceftriaxone	2(33.3)	4(66.7)	6	0.248(NS)
15	Cefotaxime	2(28.5)	5(71.5)	7	0.108(NS)
16	Ceftazidime	3(23)	10(77)	13	0.006(S)
17	Aztreonam	1(20)	4(80)	5	0.057(NS)

\*Regardless of the sample taken

\*\*These results may not reflect the true ratio because of low number of test performed.

(S) = Significant difference. (NS)= Non-significant

## Discussion

In the present settings, the ICU receives patients referred from either postoperative or critically ill due to trauma, and usually they are attached to many machines and instruments example endotracheal tube, Foley catheter, central line ...etc. which are potential sources of cross infection between patients.

In the current study, every patient received antibiotic treatment prescribed by the senior physician in charge and usually it is prescribed based on clinical basis and experience to start with, and this is what was applied in five tertiary care hospitals in Germany as stated by Wilke M *et al* who showed that therapy based on local experiences may be sufficient for patients with low complicated pathogen risk score (CPRS) but inadequate for those with high CPRS<sup>(7)</sup>.

In the present study samples for culture and sensitivity were taken from all patients on admission, but only 16 of 46 patients have their culture and sensitivity results back.

This indicates a major breakdown on the care system and implies a comprehensive review of the weak points that delay or corrupt the management line of the patients regarding treating their infections.

Also, in the present study, the mean time for culture and sensitivity results to come back to RCU was 9.58 days (range 1-27 days), this is a long period.

This problem is also a challenge in the medical practice even in the in European countries, as there is a wide difference between many countries in retrieving the results of the culture test, for example in UK, 2 hr. are needed from collection to incubation while in Germany 20 hr. are needed for incubating the bacteria due to remote laboratories<sup>(9)</sup>, still these periods are much shorter than that in our laboratories.

This is not acceptable delay and this for sure will impede or derange the course of treatment and delay the recovery of patients and may encourage resistance emergence of fatal bacterial infections.

There are many studies abroad looking for new methods to shorten the period of detecting the causative organisms in the patients so as to improve the selection of the antibiotics as early as possible and by this improve the outcome, such as a study which used new spectrometry method which provides rapid pathogen identification in critically ill patients with the ability to rule out infection within 6 hours. This has potential clinical and economic benefits<sup>(10)</sup>.

A new computer-assisted infection (CAI) monitoring software program has been developed for use in an intensive-care unit (ICU)<sup>(11)</sup>.

The commonest bacteria isolated from patients in this study was *klebsiella* (53.8%), and the least was coagulase-negative *staphylococci* (7.6%). This result differs from that of a study done in Spain which found that the microorganisms most frequently isolated in patients with inadequate empirical antimicrobial treatment were: coagulase-negative *staphylococci* (29.5%), *Acinetobacter baumannii* (27.3%), *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Proteus mirabilis*, *Escherichia coli*, and *Candida* species (4.5% each)<sup>(4)</sup>.

Whereas another study, done in Turkey found that *Pseudomonas* spp. were the most frequently isolated Gram-negative species (26.8%), followed by *Klebsiella* spp. (26.2%), *Escherichia coli*, *Acinetobacter* spp. and *Enterobacter* spp. were the other commonly isolated organisms<sup>(2)</sup>.

In the present study ceftriaxone was the main antibiotic used as an empiric treatment, this may be due to an experience with this drug, its availability, its opened dispense with no limitation and its broad spectrum of action.

Now, if we compare the results of culture and sensitivity test in the present study, we can notice clearly that 9 (90%) tests out of 10 tests done shows that tobramycin was the most effective against bacteria but it was not used clinically because it was unavailable during the period of the study. The 2<sup>nd</sup> most effective antibiotic against bacteria was ciprofloxacin and levofloxacin 9 (69.2%) sensitive tests out of 13 tests for each. While the most frequently used antibiotic in empiric treatment (ceftriaxone) was one of the least effective antibiotic on isolated bacteria 2 (33.3%) sensitive tests as revealed by culture test. This infrequent use of ciprofloxacin may explain its potential activity against isolated bacteria as revealed by culture studies, and this in turn should alert the clinicians and the clinical pharmacists to review their selections of the empirical therapy drugs and to decrease their use of ceftriaxone as first choice antibiotic in the empirical treatment.

Ceftriaxone resistance was noted by Madani N *et al* who studied the resistance of bacteria in ICU against several antibiotics and revealed that 75.0% of *Klebsiella*, 31.9% of *E. coli* and 68.4% of *Enterobacter* spp. were resistant to ceftriaxone and 10% of *Enterobacter* spp. to imipenem and 13.5% *Pseudomonas* spp. were resistant to imipenem. They concluded that bacterial resistance was high in Morocco<sup>(12)</sup>.

In contrary to the present study, the results of a study done from 2005 to 2010, showed that ciprofloxacin-resistant *E. coli* strains

(37.1%) was increased, as well as imipenem-resistant (36.4%) and ciprofloxacin-resistant (37.1%) strains of *P. aeruginosa*<sup>(13)</sup>. In another study, increasing ciprofloxacin-resistance was evident for *K. pneumoniae*<sup>(14)</sup>.

Levin PD (2007) determined risk factors associated with ciprofloxacin resistance in clinical bacterial isolates from ICU patients which includes prior use of fluoroquinolones and duration of hospitalization prior to ICU admission<sup>(15)</sup>.

Metronidazole is widely used antibiotic in our clinical practice and unfortunately the culture and sensitivity tests for anaerobic bacteria are unavailable in most of our centers including our settings in the present study, so we can't evaluate its efficacy against bacteria, but in the recent years, metronidazole has appeared to lose some of its effectiveness in *Clostridium difficile* infection (CDI) management and vancomycin is now recognized as the first-line treatment of severe cases<sup>(16)</sup>, although, many studies proved that the rate of CDI in ICU patients is low, but the infection affects severely ill patients, and is associated with high mortality<sup>(17,18,19)</sup>.

In the current study the mortality rate was 47.8%, and this is very high when compared with a study done in USA in 2009 which revealed that the mortality rate range from 9.3% to 13.3%<sup>(20)</sup>.

The high mortality rate in the present study may partly be caused by sepsis and inappropriate use of antibiotics as shown in the results.

Also another study supports claims that the availability of medical and nursing staff is associated with the survival of critically ill patients<sup>(21)</sup>.

In conclusion, there is a critical need for reviewing the trend of antibiotic use in the ICUs depending more on laboratory tests to identify the most effective drugs and to minimize the emergence of resistant infection.

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