Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 7, Issue, 01, pp.11245-11256, January, 2015

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

ANTIBIOTIC SENSITIVITY IN PSEUDOMONAS AREUGINOSA IN TAIZ, YEMEN-2013

***,[1]Fuad A. Saad and [2]Ali G. Al-Kaf**

[1]Department of Microbiology, Faculty of Applied Sciences,Thamar University,Thamar,Yemen
[2]Department of Medicinal Chemistry, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen

ARTICLE INFO

Article History:
Received 21st October, 2014
Received in revised form
17th November, 2014
Accepted 05th December, 2014
Published online 23rd January, 2015

Key words:

Pseudomonas,
β –lactam,
Yemen.

ABSTRACT

Pseudomonas aeruginosa is an important opportunistic pathogen that infects immune compromised hosts and is characterized by its natural resistance to a variety of antimicrobial agents. The purpose of this study was the assessment of the some antimicrobial sensitive level among *P. aeruginosa* clinical isolates, furthermore to compare between the different antibiotics among the susceptible and sensitivity by isolates of *P. aeruginosa* also to detect the most potent drug on *P. aeruginosa.* A total of 65 clinical isolates of *P. aeruginosa* from the patient in different laboratories in Taiz city, as following Aljomhory hospital laboratories (50) isolates, alpharaby laboratories (15) isolates. Most of the isolates were from ear followed by urine. Uropathogenic *P. aeruginosa* infections were higher in females than males, ratio was found more among young and elderly debilitated patients. The result is Ciprofloxacin, amikacin, tobramycin were found more effective as monotherapy for treatment of infections in patients. The most studied case indicate the *P. aeuroginosa* was resistant to most β-lactam particularly resist 100% to ticarcillin. In vitro sensitivity pattern of 65 isolates of *P. aeruginosa* showed highest sensitivity to ciprofloxacin (75%) followed by amikacin (65%), tobramycin (62%), and were much more resistant to β -lactam and norfloxacin antibiotics. the result of study by using combination therapy that we have use the following combinations which in all combinations are indicate to synergistic action (Ciprofloxacin+gentamycin), (Ciprofloxacin+Amikacin), (Ciprofloxacin+Ceftriaxone). Finally all the results indicate that *P. aeruginosa* is the most common gram-negative bacterium responsible for the nosocomial as well as community acquired infections. And the excessive use of antibiotics has not only led to treat the *P. aeruginosa*infections but also the emergence of antibiotic resistance.

INTRODUCTION

*Pseudomonas aeruginosa*is a gram negative bacillus, motile and belongs to the family Pseudomonacea. It has been isolated from environments as diverse as water, Jet plane fuel and disinfectant solutions due to its ability to utilize many different organic compounds and survive in the apparent absence of nutrients. A study (Costerton and Anwar, 1994) described it as the most abundant life form on earth. *P. aeruginosa*which is regarded as the most common gram-negative bacterium found in deferent systems infections has increasingly become a prevalent opportunistic human pathogen. As it can infect any external site or organ, it can be isolated in body fluids such as Urine, wounds. It is a leading cause of progressive infections, especially in critically ill and immune-compromised patients (Hugbo and Olurinola, 1992). It has been implicated in diverse infections like nosocomial pneumonia, urinary tract infection, surgical site infection, severe burns and infections of patient undergoing either chemotherapy for neoplastic disease Or those on antibiotic therapy (Basic Clinical Microbiology 1999). The mechanisms of resistance to antibiotics include reduced cell wall permeability, production of extracellular chromosomal and plasmid mediated β-lactamases (Livermore, 1989), aminoglycoside-modifying enzymes and cephalosporinases (Prince, 1986) and an active multidrug efflux mechanism. Most infection due to multidrug resistant *P. aeruginosa*has become a global health care problem since it prolongs the duration of hospitalization and increases the cost of patient care. The aim of this study is to determine the current trends of antibiotic susceptibility among *P. aeruginosa*strains causing different type infections in this environment.

Corresponding author: Fuad A. Saad
Department of Microbiology, Faculty of Applied Sciences, Thamar University, Thamar, Yemen.

MATERIALS AND METHODS

Sampling

This study was carried out during months periodstarting at 6/2011 - 8/2011. The samples are bacteria *P.earogenosa* collected from urine and ear swabs. The objective of this study was to determine the *P. aeruginosa* sensitivity pattern to commonly used antibiotics. Information regarding patient's age,

Sex, and type of specimen taken were also recorded. All the isolates were identified using colony morphology on blood agar MacConkey agar, positive reaction to oxidase, and finally by pyocyanin production (Gencer *et al.,* 2002). Antibiotic susceptibility testing was done on Mueller Hinton agar by Kirby-Bauer disc diffusion method following NCCLS recommendations(NCCLS 1997), using ceftriaxone 30 mg, gentamicin 20 mg, amikacin 30 mg, ciprofloxacin 5 mg, norfloxacin 10mg, cefotaxime 10mg (Hi-Media, Mumbai, India) and bacitracin 10mg.

Isolation of Bacteria

Bacteria isolated from patients who have urine,ear contamination by bacteria in Aljomhory hospital samples material collected was inculcated directly over the surface of media following culture media that used blood agar (Hi-Media, Mumbai, India), this medium used mainly to isolate pathogenic bacteria from the specimens and detect, hemolytic bacteria group.

Culture and Identification of Bacteria

Culture the Specimen

Inoculate the swab on blood agar medium and incubation at 35 – 37c and macConkey agar medium and can see produce pyocyanin in nutrient agar medium.

Identification the Specimen

Gram stain is used to differentiate between gram positive and negative bacteria are divided into two categories depending on whether they can be decolorized with acetone after staining with iodine. Oxidase test (Hi-Media, Mumbai, India) used for detection of oxidase production by microorganisms.

Antimicrobial Sensitivity test

Use plates with Mueller Hinton agar (M173) for use in the Bauer-Kirby (Bauer *et al.,* 1966) Method and composed of Mueller Hinton agar (Hi-Media, Mumbai, India) use for determination of susceptibility of microorganisms to antimicrobial agent. the choice of antimicrobials to be included in susceptibility tests will depend on the pathogen, the specimen, rang of locally available antimicrobials Ciprofloxacin 5mg, norfloxacin 10mg, ceftriaxone 30mg, amikacin 30mg, cefotaxime 10mg, gentamycin 20mg, bacitricin 10mg (Hi-Media, Mumbai, India),

Turbidity Standard Method

Using a sterile wire loop touch 3-5 well isolated coloniesof similar appearance to the test organism and emulsify in 3-4 ml of sterile physiological saline. In a good light match the turbidity of the suspension to the turbidity stander, using a sterile swab, evenly inoculate a plate of Mueller Hinton agar, streak the swab evenly over the medium, using sterile forceps, meddle mounted in a holder, within 30 minutes of applying the discs invert the plate and incubate it aerobically at 35c for 16-18 hr. After overnight incubation, examine the test plates. Using a ruler on the underside of the plat measure the diameter of each zone of in mm. Using the interpretative chart ,interpret the zones size of each antimicrobial, reporting the organism as resistance,intermediate or sensitive.

Tamboar Method

District laboratory practice in tropical countries parts cheese brought Monica 2000 came bridge university press 138-189 bags. This is method used to defect an relationship between tow antibiotic Procedure method, Prepare antibiotics solution.

- Gentamycin 80 mg in 2 ml → (Hi-Media, Mumbai, India)
- Ciprofloxacin 200 mg in 100 ml → (Hi-Media, Mumbai, India)
- Ceftriaxone 1000 mg in 100 ml → (Hi-Media, Mumbai, India)
- Amikacin 125 mg in 2 ml → country of origin is aspain

Prepare make paper strips then sterilize them and dry them, saturate the stripe by antibiotic, spurt the stable suspense on surface of MHA media, Put two saturated stripes on the surface of the same media, Incubate for 24hr, Read the result.

The Result

The Studies on Monotherapy

Study in laboratories of Alhekmah University:

Result of that appear when examined effect pseudomonas *aeruginosa* bybauer-kirby method

RESULTS AND DISCUSSION

Development of antibiotic resistance is of great concern. The treatment of infections caused by *P.aeruginosa* is getting more difficult because of widespread resistance, existing multi-resistance patterns, and the development of quick resistance during treatment. The determine of effective antibiotic on *P.aeruginosa* is crucial to determine the convenience of antimicrobial susceptibility tests in case infections that have been studied as following:

In monotherapy

In Table (1) Study of *P.aeurogenosa* by Baurekriby in Alhikmah university lab. This method is done by measuring the diameter of inhibition zones and the result was as following:

1- Floroquinolones have different effect by ciprofloxacin 30 mm best effect but norfloxacin25 mm (moderate effect)

2- Aminoglycosides both gentamicin and amikacin have same effect 25mm (moderate effect)
3- But β- lactam have the different action as following:
   - Cephalosporin (Ceftriaxone) has moderate effect (25 mm)
   - Bacitracin and cefotaxime (Cephalosporin) have no any effect on *P. aeruginosa*

Table 1. Study of *P.aeurogenosa* by Baurekriby in AlhikmahUniversity lab

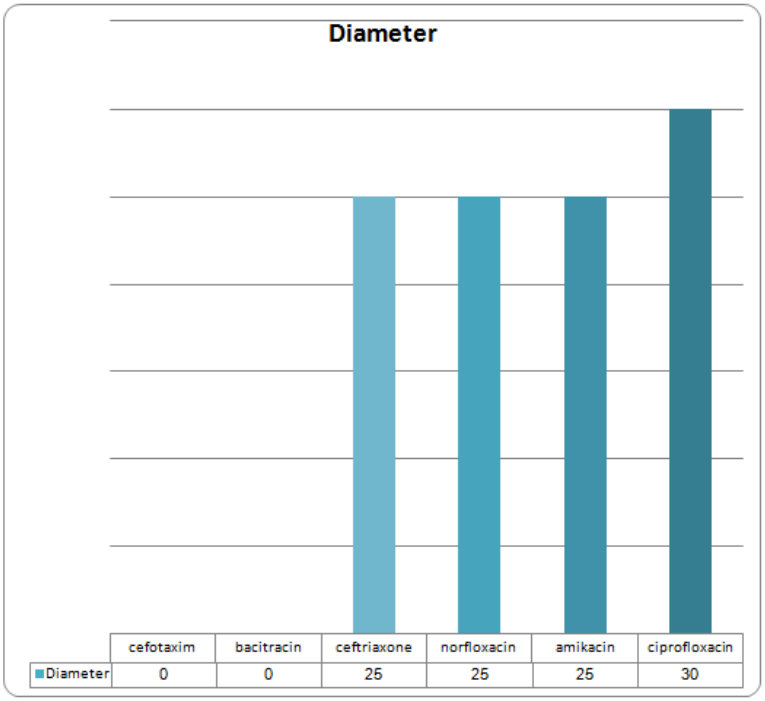
	Antibiotic	Diameter	Commended
1	Ciprofloxacin	30mm	Sensitive
2	Amikacin	25mm	Sensitive
3	Norfloxacin	25mm	Sensitive
4	Ceftriaxone	25mm	Sensitive
5	Bacitracin	0	Resistance
6	Cefotaxim	0	Resistance

From all above result we show that the bacteria *P.aeurogenosa* has highly sensitive to ciprofloxacin at monotherapy. In Table (2) study of *P.aeurogenosa* in urine in Aljomhory hospital. This study of *P.aerugenosa* in urine show the bacteria has highest sensitivity to tobramycin that frequent 5 times in 26 case studied then ciprofloxacin which frequent 4 times in 26 case studied on other hand we find that the *P.aeruginosa* has the moderate sensitivity to (ofloxacin, amikacin, minocyclinandaztreonam) all have been frequented 3 times, also moderate sensitivity to (gentamicin, netilimicin, cefotetan and doxycyclin) all have been frequented 2 times. At opposite side this study show that the bacteria *P.aerugenosa* has lowest sensitivity to others antibiotics under study. Depending on antibiotic class we show that the both floroquinolones and aminoglycosides each has different efficacy highest or moderate but most aminoglycosides drugs have moderate efficacy

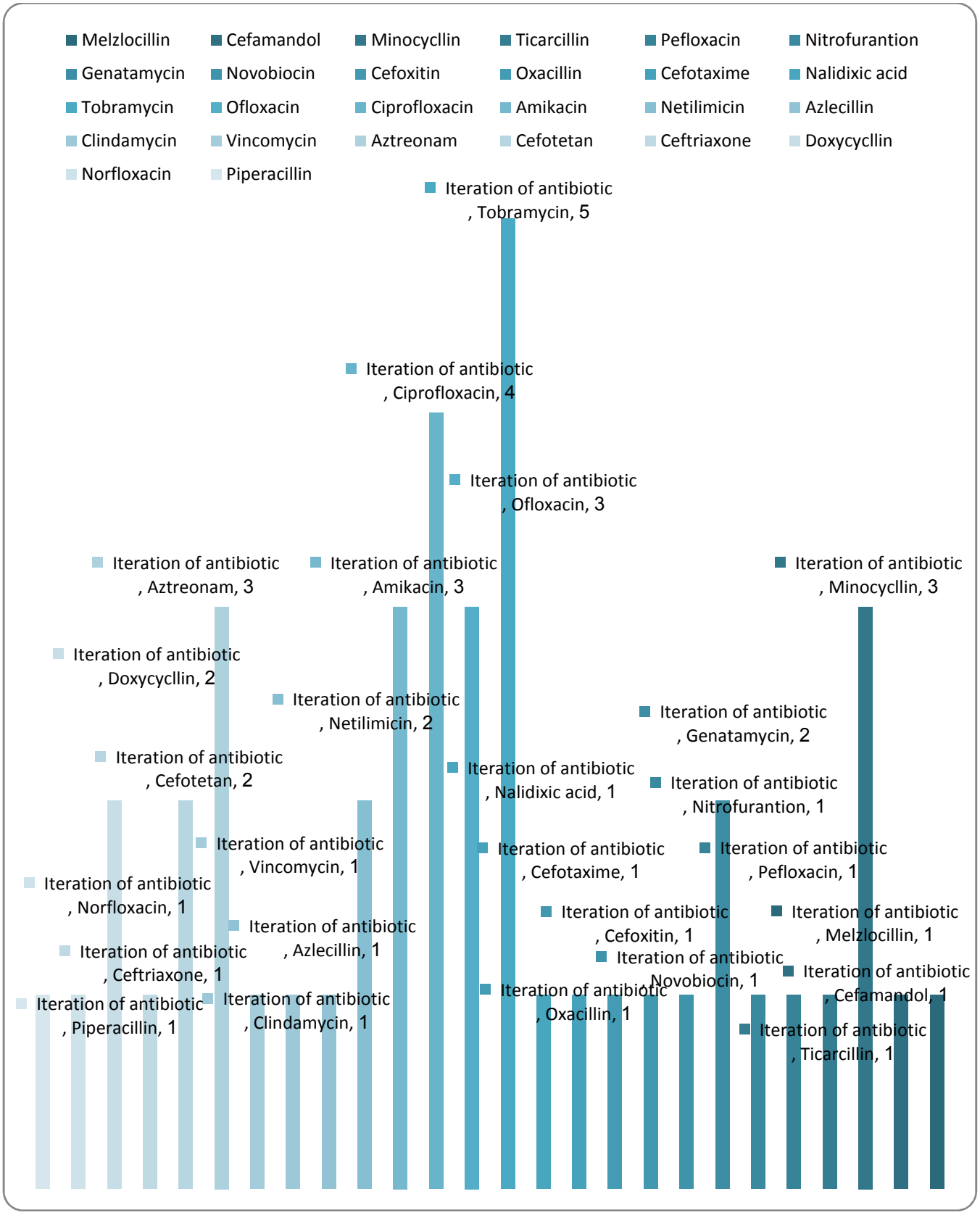
Table 2. Study of *P.aeurogenosa* in urine in Aljomhory hospital

No	Iteration of antibiotic	Antibiotic
1	1	Melzlocillin
2	1	Cefamandol
3	3	Minocycllin
4	1	Ticarcillin
5	1	Pefloxacin
6	1	Nitrofurantion
7	2	Genatamycin
8	1	Novobiocin
9	1	Cefoxitin
10	1	Oxacillin
11	1	Cefotaxime
12	1	Nalidixic acid
13	5	Tobramycin
14	3	Ofloxacin
16	4	Ciprofloxacin
17	3	Amikacin
18	2	Netilimicin
19	1	Azlecillin
20	1	Clindamycin
21	1	Vincomycin
22	3	Aztreonam
23	2	Cefotetan
24	1	Ceftriaxone
25	2	Doxycycllin
26	1	Norfloxacin
27	1	Piperacillin

whereas β-lactam class antibiotics have ether moderate or low efficacy but the most patterns have low efficacy. In Table (3) study of *P.aeurogenosa* in ear in Aljomhory hospital: This study shows that the bacteria *P.aerugenosa* in ear have highest sensitivity to ciprofloxacin, tobramycin, ofloxacinand norfloxacin. when ciprofloxacin that frequent 25 times in 30 case studied then tobramycin that frequent 22 times in 30 case studied, ofloxacin and norfloxacin both are frequented 19 times in 30 case studied.



Samples collected from the central laboratory in Aljomhory hospital: Sample in urine



This study of *P.aerugenosa* in urine show:

- the bacteria has greatest sensitivity to tobramycin then to ciprofloxacin
- has the moderate sensitivity to (ofloxacin, amikacin, minocyclin and aztreonam) then to (gentamicin, netilimicin, cefotetan and doxycyclin)
- finally this study show that the bacteria P.aerugenosa has lowest sensitivity to others antibiotics under study

1- Sample inEar

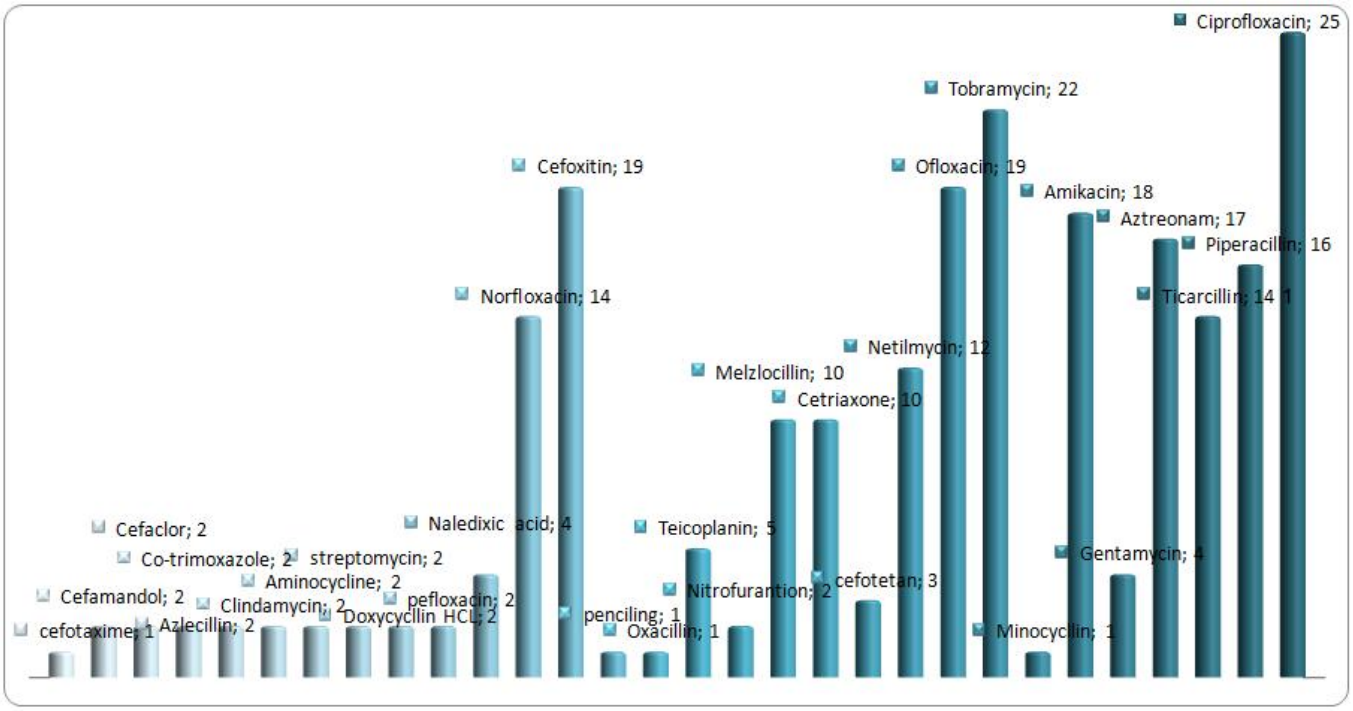
Table 3. Study of *P.aeurogenosa* in ear in Aljomhory hospital

No	Iteration of Antibiotic in ear	Antibiotic
1	25	Ciprofloxacin
2	16	Piperacillin
3	14	Ticarcillin
4	17	Aztreonam
5	4	Gentamycin
6	18	Amikacin
7	1	Minocycllin
8	22	Tobramycin
9	19	Ofloxacin
10	12	Netilmycin
11	3	cefotetan
12	10	Cetriaxone
13	10	Melzlocillin
14	2	Nitrofurantion
15	5	Teicoplanin
16	1	Oxacillin
17	1	penciling
18	19	Cefoxitin
19	14	Norfloxacin
20	4	Naledixic acid
21	2	pefloxacin
22	2	Doxycyclin HCL
23	2	streptomycin
24	2	Aminocycline
25	2	Clindamycin
26	2	Co-trimoxazole
27	2	Azlecillin
28	2	Cefaclor
29	2	Cefamandol
30	1	cefotaxime

1-Sample in different space

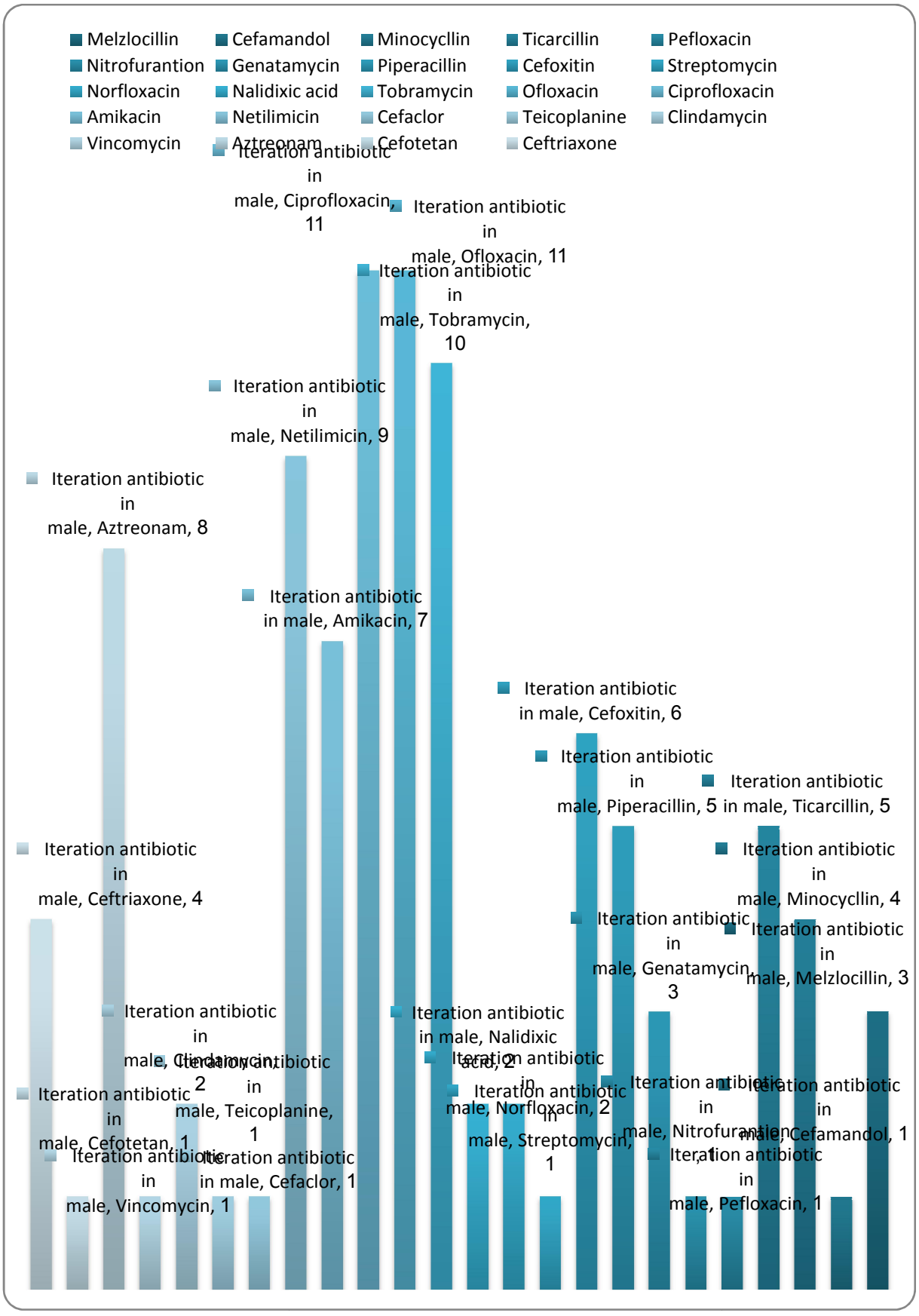
a-Sample Male

	Iteration Antibiotic in male	Antibiotic
1	3	Melzlocillin
2	1	Cefamandol
3	4	Minocycllin
4	5	Ticarcillin
5	1	Pefloxacin
6	1	Nitrofurantion
7	3	Genatamycin
8	5	Piperacillin
9	6	Cefoxitin
10	1	Streptomycin
11	2	Norfloxacin
12	2	Nalidixic acid
13	10	Tobramycin
14	11	Ofloxacin
15	11	Ciprofloxacin
16	7	Amikacin
17	9	Netilimicin
18	1	Cefaclor
19	1	Teicoplanine
20	2	Clindamycin
21	1	Vincomycin
22	8	Aztreonam
23	1	Cefotetan
24	4	Ceftriaxone



This study of *P.aerugenosa* in ear show

- greatest sensitivity to ciprofloxacin then to tobramycin then to ofloxacin)
- has the moderate sensitivity to (amikacin, cefoxitin, aztreonamand pepracillin)
- finally this study show that the bacteria *P.aerugenosa* has lowest sensitivity to others antibiotics under study



This study of *P.aerugenosa* in urine and ear in male show:

- The bacteria has greatest sensitivity to ofloxacin and ciprofloxacin then to tobramycin
- Has the moderate sensitivity to (netilimicin, amikacin, aztreonam, cefoxitine) respectively.
- Finally this study show that the bacteria *P.aerugenosa* has lowest sensitivity to others antibiotics under study

a-Sample In Female

	Iteration of Antibiotic in Female	Antibiotic
1	4	Cefotetan
2	21	Ciprofloxacin
3	9	Mezlocillin
4	12	Ticarcillin
5	4	Cefotaxim
6	15	Aztreonam
7	4	Gentamycin
8	16	Netilmicin
9	18	Amikacin
10	1	Novobiocin
11	14	Cefoxitin
12	2	Oxacillin
13	4	Minocyellin
14	3	Nalidixic acid
15	18	Tobramycin
16	1	Ofloxacin
17	12	Pipracillin
18	2	Teicoplanin
19	2	Clindamycin
20	7	Ceftriaxone
21	1	Nitrofurane
22	1	Penicillin G
23	13	Norfloxacin
24	10	Ofloxacin
25	2	Pefloxacine
26	5	Doxycycllin
27	2	Co-trimoxazole
28	3	Teicoplanine
29	2	Azlocilline
30	1	Strptomycin
31	1	Cefaclor
32	1	Cefamandole
33	1	Nitrofurantoin

Has the moderate sensitivity to, cefoxitin,

amikacin, pepracillin and aztreonam. First cefoxitine frequented 19 times in 30 case studied then amikacin which frequented 18 times in 30 case studied, azteonam frequented 17 times in 30 case studied and pepracillin frequented 16 times in 30 case studied.Finally this study show that the all other antibiotics have low efficacy on 30 cases studied of bacteria *P.aerugenosa.* Depending on antibiotic class we show that the floroquinolones (ciprofloxacin and ofloxacin) have moderate efficacyand aminoglycosides drugs have different efficacy highest or moderate efficacy whereas β-lactam class antibiotics have ether moderate or low efficacy.

In Tab (4) study of *P.aeurogenosa*in ear in Alpharbi laboratory:

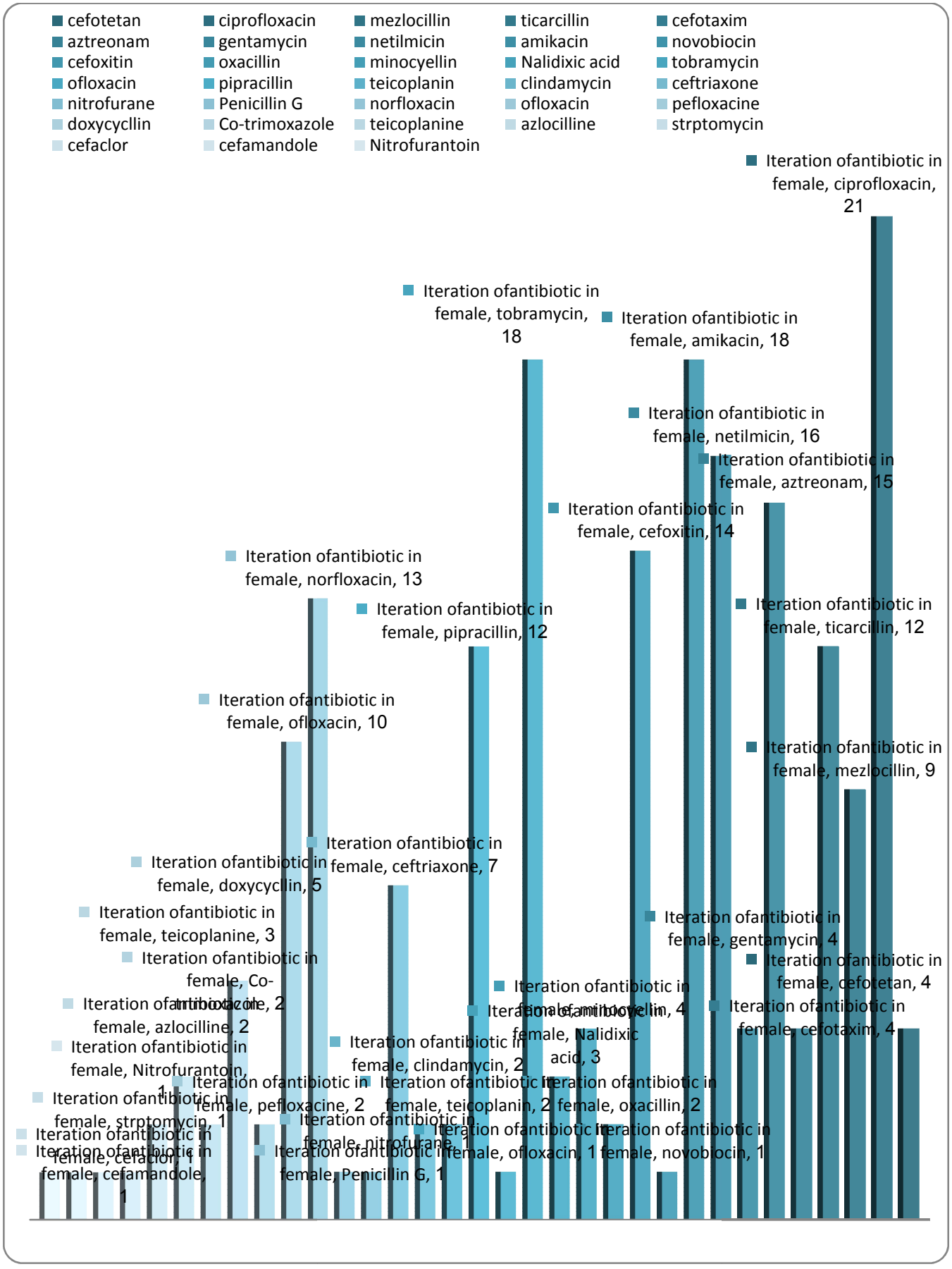
This study show that the bacteria *P.aerugenosa* in ear has highest sensitivity to gentamicin, amikacin and ceftriaxone, in gentamicin we see the drug is frequented 9 times in 11 case studied, amikacin has frequent 8 times in 11 case studiedthen ceftriaxone (β-lactam) has frequent8 times in 11 case studied moderate sensitivity is showed to cefotaxim (β-lactam), ofloxacin (floroquinolons), but the cefotaxime is frequent 7 time in 11 cases have been studied more than ofloxacin, ciprofloxacin (floroquinolons) frequent 3,2 time respectively in 11 case have been studied finally this study show that the bacteria *P.aerugenosa* has lowest sensitivity to others studied antibiotics most of these drug are β-lactam.

From table above we see The bothgroup of Aminoglycosides and Quinolones each has high efficacy on bacteria *P. aeruginosa* each group have totally the same degree of efficacy but the B-lactams have low efficacy. This is due to the mechanism of action of the drug. this mean the drugs that the drugs that inhibit protein synthesis, or Inhibit bacterial DNA synthesis by inhibiting DNA gyrase have more efficacy than that inhibit cell wall synthesis because most them especially cefotaximehydrolyzable by constitutively produced β-lactamase from the two groups that have high efficacy on bacteria *P.aeruginosa* we see:

- In Quinolones the best drug that have high efficacy on bacteria *P.aeruginosa* in group is ciprofloxacin and the lowest is norfloxacin this due to:
-
  - Norfloxacin is the least active of the fluoroquinolones against both gram-negative and gram-positive organisms, with minimum inhibitory concentrations (MICs) fourfold to eightfold higher than those of ciprofloxacin.
  - Ciprofloxacin possessing excellent gram-negative activity and MICs for gram-negative bacilli including pseudomonas is 1-2 mcg/mL and often less. For that Ciprofloxacin is the most active agent of Fluoroquinolones against gram-negatives, *P. aeruginosa* in particular.
  - In general, none of 2nd generation agents is as active as ciprofloxacin against gram-negative organisms (Basic and Clinical Pharmacology - 10th Ed. (2007)45

in Aminoglycosides the best drug in group is amikacin and the lowest is gentamicin:

- Gentamicin is active alone, but also as synergistic companion with β-lactam antibiotics against pseudomonas gram-negative rods that may be resistant to multiple other antibiotics but Among gram-negative bacteria, resistance is most commonly due to plasmid-encoded aminoglycoside-modifying enzymes. But these bacteria are susceptible to amikacin, which is much more resistant to modifying enzyme activity (Basic and Clinical Pharmacology- 10th Ed. (2007)45.
- Tobramycin has almost the same antibacterial spectrum as gentamicin with a few exceptions: tobramycin is slightly more active against pseudomonas. Although there is some cross-resistance between gentamicin and tobramycin.
- Amikacin It is resistant to many enzymes that inactivate gentamicin and tobramycin, and it therefore can be used against some microorganisms resistant to the latter drugs. Many gram-negative enteric bacteria including pseudomonas are inhibited BY peak levels in serum are 10-30 mcg/mL. (Basic and Clinical Pharmacology - 10th Ed. (2007)45



This study of *P.aerugenosa* in urine and ear in female show:

- the bacteria has greatest sensitivity to ciprofloxacin then to tobramycin then to amikacin) respectively
- The bacteria has the moderate sensitivity to (netilimicin, aztreonam, cefoxitine, pepracillin) respectively.
- Finally this study show that the bacteria P.aerugenosahas lowest sensitivity to others antibiotics under study.

i. Alpharbi laboratory

a. Sample in Ear

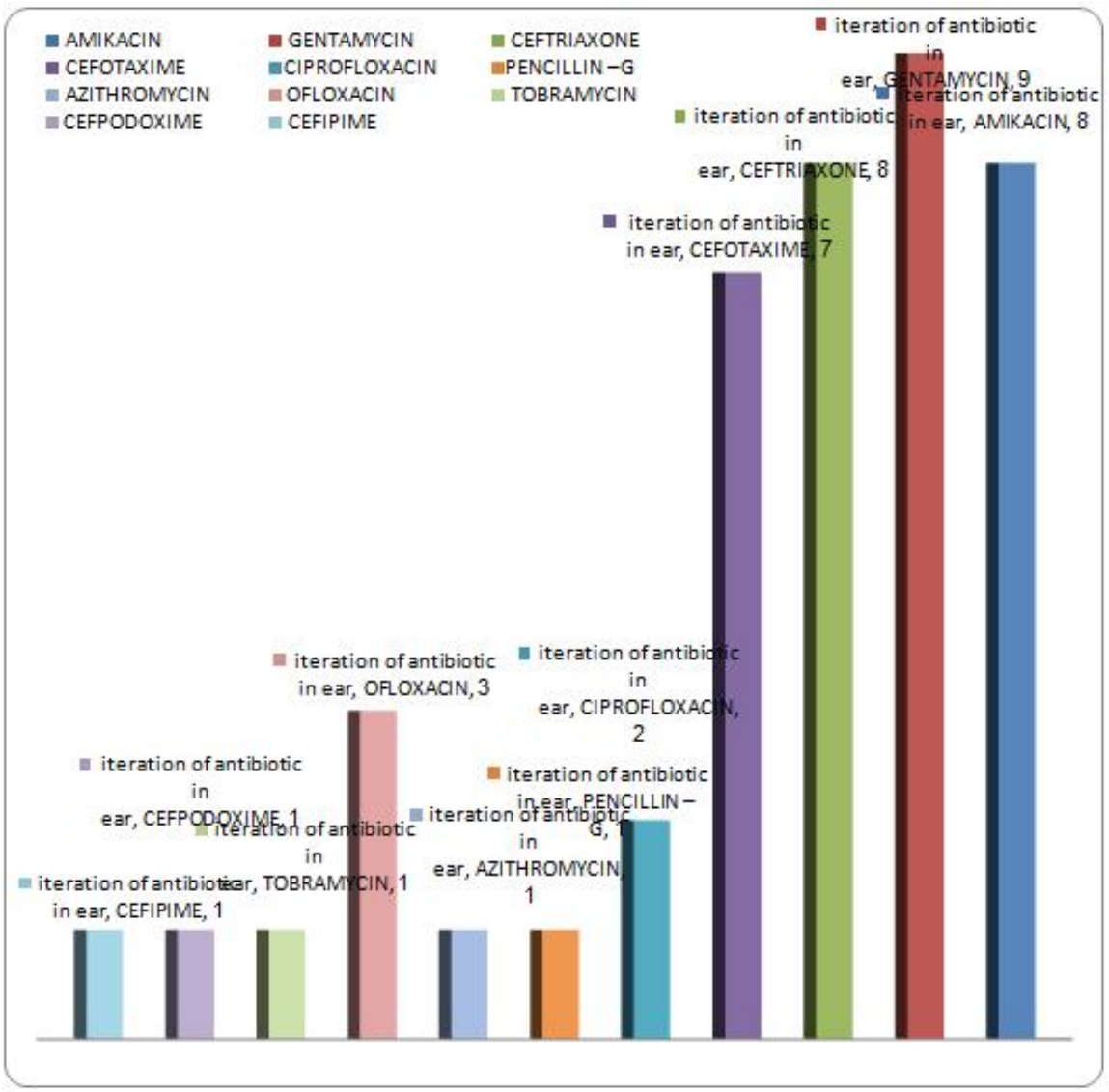
ii. Table 4. Study of *P.aeurogenosa* in ear in Alpharbi laboratory

	Iteration of Antibiotic in Ear	Antibiotic
1	8	Amikacin
2	9	Gentamycin
3	8	Ceftriaxone
4	7	Cefotaxime
5	2	Ciprofloxacin
6	1	Pencillin –G
7	1	Azithromycin
8	3	Ofloxacin
9	1	Tobramycin
10	1	Cefpodoxime
11	1	Cefipime

b. Sample in Female

	Iteration of Antibiotic in Female	Antibiotic
1	3	Amikacin
2	3	Gentamamicin
3	3	Ceftriaxon
4	1	Ofloxacin
5	1	Cefpodoxime
6	3	Cefotaxim
7	1	Cefipime

Iteration of Antibiotic in Male



This study collected from *P.aerugenosa* in different part in male and show :

- greatest sensitivity to gentamicin then to amikacin then to ceftriaxone)
- has the moderate sensitivity to (cefotaxim, ofloxacin)
- finally this study show that the bacteria *P.aerugenosa* has lowest sensitivity to others antibiotics under study

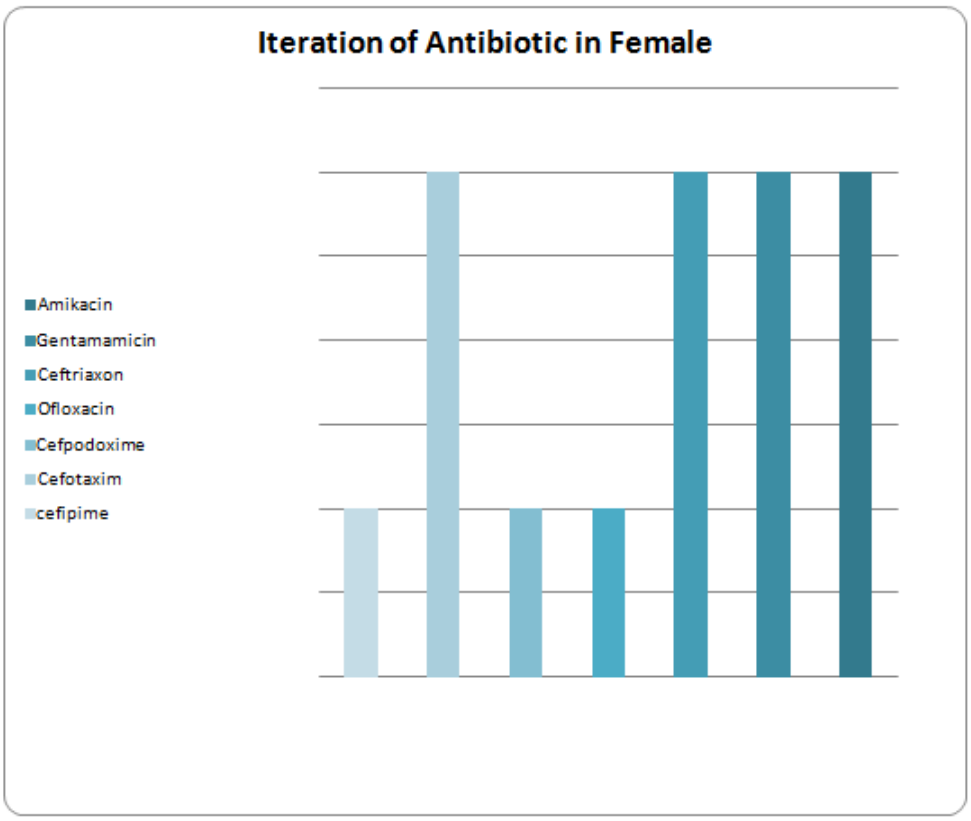


Table 5. Study theeffect of combination antibiotic on *P.areuginosa*by tambour method

Antibiotic	Commended
Ciprofloxacin + Gentamycin	Synergism
Ciprofloxacin + Amikacin	Synergism
Ciprofloxacin + Ceftriaxone	Synergism

*This study show that the three different combinations have syngisticaction

Table 6.Showing the total result about our study

	class	Subclass	drug	Type of sensitivity			Total group result		
				High	Mod	Low	High	Mod	Low
1	B-lactams	Cephalosporin	Ceftriaxone	1	1	2	1	4	7
			Cefotaxime	0	1	3			
			Cefixitine	0	2	2			
		penicillin's	Ticarcillin	0	0	4	0	3	9
			Piperacillin	0	1	3			
		Monobactams	Aztreonam	0	2	2			
2	Aminoglycosides		Gentamicin	1	1	2	4	4	4
			Amikacin	1	3	0			
			Tobramycin	2	0	2			
3	Quinolones		Ciprofloxacin	3	0	1	4	2	6
			Ofloxacin	1	1	2			
			Norfloxacin	0	1	3			

Finally from above discuss to two groups (aminoglycosides and floroquinolons) we show:
That the ciprofloxacin (fluoroquinolones) has highest efficacy against *p.aeruginosa* than amikacin (aminoglycosides) and we analyze the reasons as flowing:

Aminoglycosides

Aminoglycosides have concentration-dependent killing, that is, increasing concentrations kill an increasing proportion of bacteria and at a more rapid rate. They also have a significant post antibiotic effect, such that the antibacterial activity persists beyond the time during which measurable drug is present. The post antibiotic effect of aminoglycosides can reach several hours. Because of these properties, a given total amount of aminoglycoside may have better efficacy when used as a single large dose than when administered as multiple smaller doses (45 Basic and Clinical Pharmacology - 10th Ed. (2007).

Fluoroquinolones

Fluoroquinolones were originally developed because of their excellent activity against gram-negative aerobic bacteria. Clinically, the fluoroquinolones are best used for infections with facultative and aerobic Gram-negative rods and cocci.* Resistant strains of *S. aureus* and *P. aeruginosa* have emerged. Ciprofloxacin has a wide antibacterial spectrum, being especially active against Gram-negative enteric coliform organisms including many organisms resistant to penicillin, cephalosporin and aminoglycosides (pharmacology 5th edition range and dale). After oral administration, the fluoroquinolones are well absorbed (bioavailability of 80 95%) and distributed widely in body fluids and tissues, Serum half-lives range from 3 to 10 hours. Ciprofloxacin (fluoroquinolones) is eliminated by renal mechanisms, either tubular secretion or glomerular filtration (Basic and Clinical Pharmacology - 10th Ed. (2007)46.

i- In combination therapy

Table (5) study the effect of combination antibiotic on *P.areuginosa* by tambour method.

In three combination the study show:

Ciprofloxacin + Ceftriaxon not preferred because the ciprofloxacin hashigh activity but Ceftriaxon has moderate activity also sensitivity to β-lactamase.

Ciprofloxacin + gentamycin not preferred because the ciprofloxacin has high activity but gentamycin has the lowest activity in AMGSs group also gentamycin more side effect than amikacin.

Ciprofloxacin + Amikacin is the best combination because the two drug are the highest activity in their groups also there are no problem or drug- drug interaction between them depending on (Stockley's Drug Interactions ,Karen Baxter (in bags 37 , 403).

Conclusion

This work describes an assessment of a of sensitivity level of antibiotic on *P.aeruginosa* isolate. The study confirm that the Bactria *P.aeruginosa* is predominant problem for most patient and physicians. Our results indicate that the frequency of antibiotics sensitivity in combination therapy is more than that in monotherapy. The *P.aeruginosa* resist for most antibiotic when administrated as a monotherapy except few patterns of floroquinolons and aminoglycosides. These finding indicates the existing gap between current laboratories practice and the desired goal of the effectiveness treatment. Ciprofloxacin + Amikacin is the best combination because the two drug are the highest activity in their groups also there are no problem or drug- drug interaction between them depending on (Stockley's Drug Interactions, Karen Baxter (in bags 37, 403). The underlying resistance of *Pseudomonas aeruginosa* to several antibiotics could be a contributory factor To overcome the latter, several studies indicate that a combination of antibiotics is the preferable therapy for severe *Pseudomonas aeruginosa* infections.

REFERENCES

A b "Research could lead to new non-antibiotic drugs to counter hospital infections" (Press release). University of Chicago Medical Center. 2009-04-14. Retrieved 2010-01-18.

A b AVI Biopharma (2007-01-18). "Antisense antibacterial method and compound". World Intellectual Property Organization. Retrieved 2008-10-18.

Al-Rahawi and AL-Kaf, textbook of medicinal and Pharmaceutical Chemistry (first edition)2009

Antimicrob agent Chemother 1997 May;41(5):1127-33

Anzai; Kim, H; Park, JY; Wakabayashi, H; Oyaizu, H (2000, Jul). "Phylogenetic affiliation of the pseudomonads based on 16S rRNA sequence". *Int. J. Syst. Evol. Microbiol.,* 50 (4): 1563–89.doi:10.1099/00207713-50-4-1563. PMID 10939664.

Basic Clinical Microbiology. Abkara, Gunes Publication, 1999, pp 551-558.

Bauer AN, Kirby WMM, Sherris J, *et al.*1966. Antibiotic susceptibility testing by a standardized single disk method. *Am. J.Clin.Pathol.,*45: 493-6.

Bodey, G.P, Jadeja, L, Elting, L. Pseudomonas bacteremia. Retrospective analysis of 410 episodes.*Arch. Intern. Med.,* 1985; 145:1621.

Clin Lab Sci. 2011;24(1):52

Clinical drug therapy, Anne collinsabrams, j.b.lippincott company (Third edition)

Costerton,J.W., H. Anwar. *Pseudomonas aeruginosa* the microbe and pathogen *Pseudomonalaeruginosa*: Infections and treatments, edsBaltich AL, Smith RP, Marcel D, New York, 1994, pp 1-20

Edmond and Sahm *et al.* 1999

Essentials of Medical Pharmacology,Tripathi KD: Indian Basic and clinical pharmacology (Book) by Bertram G. Katzung, Susan B. Masters, *Anthony J. Trevor - McGraw-Hill Medical,*(2009.07.01)

Gencer, S., Oznur, A.K., Benzonana, N., Batrel, A., Ozer, S. 2002. Susceptibility patterns and cross resistances of antibiotics against *P.aeruginosa* in a teaching hospital of Turkey. *Ann.Clinmicrobiol.Antimicrob.,* 1:2

Goodman and Gilman's the pharmacological basis of therapeutics (by Louis Sanford Goodman, Alfred Gilman, Laurence L. Brunton, John S. Lazo, Keith L. Parker - McGraw-Hill (2006) -A Doody's Core Title ESSENTIAL PURCHASE! 5 STAR DOODY'S REVIEW! "The 11th edition

Hamilton-Miller and Brumfitt, 1981

Hilf, M, Yu, VL, Sharp, J, *et al.*Antibiotic therapy for *Pseudomonas aeruginosa* bacteremia: outcome correlations in a prospective study of 200 patients.*Am. J. Med*., 1989; 87:540

Hugbo,P.G. and P.F. Olurinola. Resistance of *Pseudomonas aerug*inosa to antimicrobial agents:

Implications in medicine and pharmacy. Nig. Journ. Pharm. Sci. 4: 1-10 (1992).

Iglewski BH (1996). Pseudomonas. In: Baron's Medical Microbiology (Baron S *et al.* eds.) (4th ed.). Univ of Texas Medical Branch. ISBN 0-9631172-1-1.

Itah A. Y. and J. P. Essien 2005. "Growth Profile and Hydrocarbonoclastic Potential of Microorganisms Isolated from Tarballs in the Bight of Bonny, Nigeria". *World Journal of Microbiology and Biotechnology*, 21 (6–7): 1317–1322. doi:10.1007/s11274-004-6694-z.

King, E.O., Ward, M.K. and Raney, D.E.1954. "Two simple media for the demonstration of pyocyanin and fluorescein". *J. Lab.Clin. Med.,* 44 (2): 301–7. PMID 13184240.

Livermore, D.M. 1989. Role of betalactamase and impermeability in the resistance of *Pseudomonas aeruginosa*. *J. Antimicrob. chemother*. 42: 257-63.

Medical Pharmacology at a Glance, 6th Edition (Michael J. Neal (United Medical and Dental Schools of Guy's and St Thomas's Hospital)

NCCLS. 1997. Performance standards for antimicrobial disc susceptibility tests. NCCLS: Wayne PA; M2-A6.

Ornelis P (editor). (2008). Pseudomonas: Genomics and Molecular Biology (1st ed.). Caister Academic Press. ISBN 1904455190.

Pharmaceutical and Biological Sciences, Aston University, Aston Triangle, Birmingham B4 7ET, UK Correspondence to: P A Lambert

Prince,A. 1986. Antibiotic resistance of pseudomonas species. *J. Paediatr.*, 108: 830-4.

Rang and Dale's pharmacology (Book) by H. P. Rang, M. Maureen Dale - Churchill Livingstone (2007.01.25)

Ryan KJ, Ray CG (editors) 2004. Sherris Medical Microbiology (4th ed.). McGraw Hill. ISBN 0-8385-8529-9.

Todar's Online Textbook of Bacteriology. Textbookofbacteriology.net (2004-06-04). Retrieved on 2011-10-09.

****