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Irrational Antibiotics use in Iraq al-Sadr Teaching Hospital - Maysan an example

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ABSTRACT

This study is retrospective study to the culture and sensitivity test that done in the laboratory of Al-Sadr hosp. in 2012, during this period about 2664 C&S tests for all types of infection this includes (1033 for urine), (790 t for blood), (250 ts for ear swab) and (591 ts for sputum) There is a completely irrational use of antibiotics in al-Sadr teaching hospital in Maysan –Iraq because there is no a clear strategy for the treatment of different infections so they use antibiotics as a prophylaxis for all patients specially Ampiclox and Claforan or ceftriaxone, but in fact there is about 14% only of patient that are suspected to be infected have a bacterial growth according to culture and sensitivity tests. Also there is only 0.4% of microorganisms that cause infection in that hospital sensitive to penicillin due to increase the antimicrobial resistance due to the overuse and misuse of antibiotics specially Ampiclox. Also the antibiotics cost is very high compared to other hospital in the neighboring countries penicillins and most of cephalosporins are no longer drug of choice for most of bacterial infections including staphylococcus bacterial infections in Iraq due to excessive use of them most of the medical problems that thought to be caused by bacterial infections, they are not. Only about 14% of them are caused by bacteria there is no critical need for antimicrobial prophylaxis for most of cases

Keywords: irrational antibiotic, antibiotics resistance, culture and sensitivity test, cost of antibiotics.

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INTRODUCTION

Antibiotics misuse and abuse leads to shortage

The consumption of antibiotics in human medicine can be measured in thousands of tons:• In Europe (29 countries), the overall human consumption was 3,350 tons in 2007.¹• In the USA, 3,300 tons were sold for human consumption in 2009.²However, half of this antibiotic consumption is unnecessary³, and greatly contributes to increasing bacterial resistance. According to Professor Schlemmer, President of the French Working Committee ‘Keep Antibiotics’, “This is a cultural issue, and it is going to take 10 or perhaps 20 years to change attitudes, but we are heading for a catastrophe if we don’t succeed⁴”

.Today, microbial resistance to antibiotics is on the rise, while the development of new antibiotics is practically at a standstill. There is a strong likelihood that curbing infections, which are hospital associated or prevalent in the community, will no longer be possible. Antibiotics have now become an endangered species that must be protected.

Looming antibiotic shortage

The new molecules that are now being developed will not be available before 5-10years, while other antimicrobials are no longer on the market, or are no longer efficient. Developing antibiotics is a complex and costly process for the pharmaceutical industry and the return on investment is considered insufficient. Protecting antibiotics is similar to protecting the environment

The overuse of antibiotics accelerates microbial resistance causing irreversible damage. Much like pollution, the effect of inappropriate use of antibiotics is not immediately perceptible and continues if it isn’t regulated. The behavior of irresponsible individuals who encourage this overuse will have an irreversible impact on the community.⁵ Antibiotics should not be wasted. They are rare and precious commodities that should be used only when appropriate.

Antibiotic resistance causes therapeutic failures that lead to death

In Europe, approximately 25,000 people die each year from infections due to five drug-resistant organisms. Infections due to these multidrug-resistant bacteria result in extra healthcare costs and productivity losses of at least EUR 1.5 billion each year.⁶

In the USA, there were nearly 900,000 cases of antibiotic-resistant infections in 2000.⁷ Methicillin-resistant *Staphylo coccus aureus* (MRSA) is estimated to be responsible for 19,000 deaths annually.⁸ A single case of MRSA can cost more than \$60,000 to treat.⁹ The estimated annual cost of antibiotic resistance for US hospitals is more than \$20 billion.^{10, 11}

This problem has increased with the emergence of ultra-resistant Gram-negative bacteria Producing enzymes such as ‘New Delhi’ metallo-beta-lactamase.¹²

Antibiotics are ineffective against viral infections, and yet they are often prescribed for respiratory illnesses such as colds or the flu, caused by viruses that will not respond to antibacterial drugs. In the absence of a clear diagnosis, physicians often prescribe antibiotics just to be on the safe side or to prevent possible secondary bacterial infections. In addition, physicians often prescribe antibiotics under pressure from patients:

In an American survey, nearly half (48%) of respondents indicated that they expected an antibiotic when they visited a doctor for a bad cold.¹³ In another survey, more than 50% of French interviewees expected an antibiotic for the treatment of flu.¹⁴

Patients are unaware of the risks associated with antibiotic misuse

Patients do not comply enough with the prescribed antibiotic treatment. They often forget to take medication, do not take the appropriate dose or may be unable to afford the full course. They tend to consider antibiotics as antipyretics that treat fever (like aspirin), and therefore stop taking them as soon as they feel better.

Self-medication is also an important driver of antimicrobial overuse, especially in countries with low or medium income, where antibiotics can be bought over the counter in pharmacies or even in local market places.

In Mongolia, for instance, even though antibiotics are not to be sold over the counter, 42% of the children are given antibiotics without prescription for respiratory tract infections.¹⁵ - But self-medication has also been noted in the United States¹⁶ and Europe,^{17, 18} particularly for colds and upper respiratory tract syndromes, which are self-limiting and mostly caused by viruses.

Sales via the internet drive self-medication; they are on the rise and difficult to control.¹⁹ Antibiotics can have adverse effects. According to the Centers for Disease Control and Prevention, 150,000 patients per year are estimated to present to US emergency departments for antimicrobial-related adverse events.²⁰

Antibiotics can be considered as “endangered species” and must be

Protected through appropriate and accurate use. Clinical lab tests are central to this effort:

Finding the exact germ which caused the infection and its sensitivity to antibiotics helps doctors prescribe the appropriate treatment.

Several clinical trials, particularly in the US, have shown that patient education can effectively change, to varying degrees, the use of antibiotics.^{21, 22}

The European Union has established a strategy to fight antimicrobial resistance and encourage the prudent use of antibiotics in human medicine. Several countries have launched national campaigns to educate physicians and patients about antimicrobial misuse and the threat of resistance.

The French campaign often held up as a model, exceeded expectations with a 26.5% reduction in the number of antibiotic prescriptions over the first five-years.²³ However France still remains a high user of antibiotics, behind Greece and Cyprus. In Belgium, antibiotic prescriptions decreased by 36% after an information campaign.²⁴

Some national campaigns (e.g. in Greece, Spain, England, Australia) failed to show a major impact on antibiotic prescriptions.²⁵

The general public still has preconceived ideas concerning antibiotics and their effects despite numerous information campaigns. For example, 53% of Europeans still believe that antibiotics kill viruses and 47% believe that they are effective against colds and flu, according to a survey published in 2010.²⁶

However, large variations between countries are observed. WHO calls on all key stakeholders around the world, including policy-makers and planners, the public and patients, practitioners and prescribers, pharmacists and dispensers, and the pharmaceutical industry, to develop and take actions to preserve this invaluable resource for public health.

The emergence of resistant bacteria is a natural phenomenon, which has been accelerated and amplified by the inappropriate use of antibiotics. Bacteria either adapt to an environment or disappear. When exposed to antibiotics, most susceptible bacteria are eliminated. Some bacteria, however, are able to adapt and survive by acquiring “resistance genes”, which result from the mutation of existing genes or from the acquisition of new genes. Resistance genes are generally located on fragments of circular DNA, called plasmids, which transfer easily from one bacterium to another. Resistance thus spreads horizontally, because it is transmitted between bacteria exchanging genetic material, but also vertically, because the bacteria multiply rapidly and transmit resistance genes to their lineage.

During the third edition of the World HAI Forum organized by bioMérieux from June 27-29 at the Pensières Conference Center in Annecy, Professor Stephan Harbarth, associate professor and hospital epidemiologist at Geneva University Hospitals, will talk about the overuse of antibiotics and its impact on bacterial resistance. Professor Harbarth will present the cultural, behavioral, economic and political factors that influence the patient-doctor relationship, and how this differs

from one country to another. The presentation will also highlight the ways and means available to doctors to avoid unnecessary prescription of antibiotics.

Irrational Antibiotics Use is include

- No indication
- Improper dosage or dosage interval
- Unnecessary or improper combination
- Improper beginning time for prophylaxis or improper duration of treatment
- Incorrect choice of AB
- More expensive and toxic drug
- Any combination of the above

Normal and pathogenic flora

Colonization inhibition: normal F compete with pathogenic M.O. for nutrients and space Normal Flora produces toxins that harmful to some pathogenic M.O. The presence of normal flora can affect the environment to become less suitable to colonization by pathogenic Mode crease the PH of the vagina and intestine so prevent the colonization of large number of pathogenic M.O.

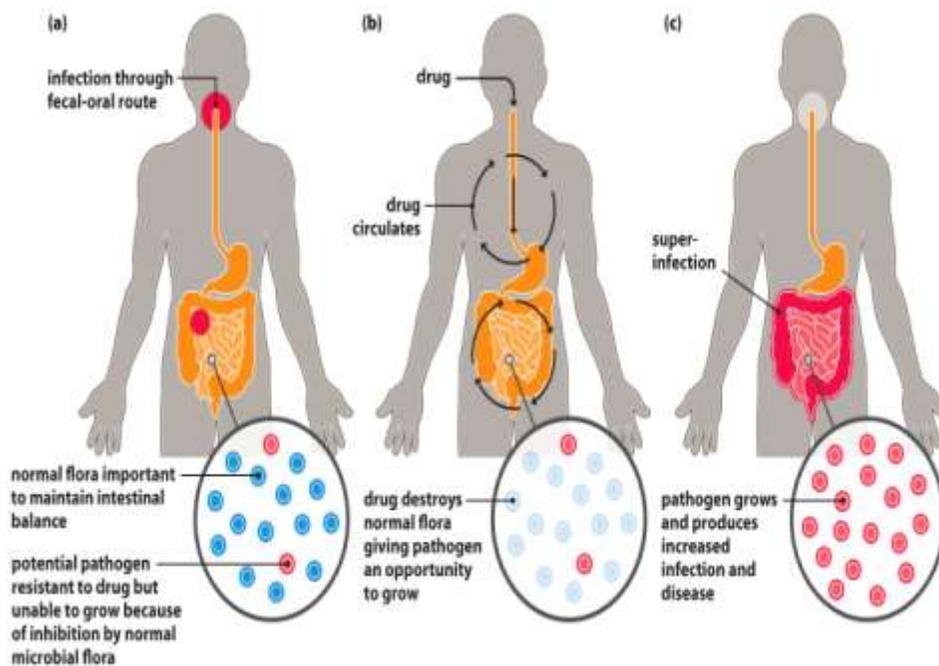


Figure :1 The competition between normal and pathogenic flora to prevent diseases, (a) the potential pathogen unable to grow because of inhibition by normal flora .(b) when antibiotic administered ,it will destroy normal flora giving an opportunity to pathogenic one to grow, (c) super-infection ;pathogen grows and produces infection and disease

Normal flora functions

- Synthesize and excrete vitamins(K,B12)
- Prevent colonization of PMO
- Stimulate the development of certain tissue in GIT (payer's patches)
- Immunity stimulation
- Stimulate the production of natural antibody ; stimulate the production of cross-reactive antibodies "antigenic priming" (induce immunological response/ natural antibodies)
- Digestion of polysaccharides in GIT

Why is an antibiotic policy necessary?

An antibiotic policy will:

- improve patient care by promoting the best practice in antibiotic prophylaxis and therapy,
- Make better use of resources by using cheaper drugs where possible retard the emergence and spread of multiple antibiotic-resistant bacteria.
- improve education of junior doctors by providing guidelines for appropriate therapy eliminate the use of unnecessary or ineffective antibiotics and restrict the use of expensive or unnecessarily powerful ones

Function of the antibiotic committee

To consult widely with the clinical staff to get agreement on antibiotic usage in different specialties to then establish an antibiotic formulary, which may prevent the use of some drugs and restrict the use of others to formulate guidelines for antibiotic prescribing, including indications for prophylaxis and therapy of infection, the optimum dosages, timings and duration of therapy and policies for minimizing the risks of toxicity to review the appropriateness of antibiotic use and the emergence of antimicrobial resistance and provide feedback on this to clinicians to be responsible for education and dissemination of information to work closely with the Infection Control Team and the Microbiology Department

The Key Members of the Antibiotic Committee

If possible, the following key persons should be included in the committee:

- The Pharmacist who will report back to the Antibiotic Committee at each meeting on drug utilization and cost.
- The Microbiologist who will report on antibiotic susceptibility patterns of bacteria isolated from major infections.

- Clinical doctors, pharmacist and nurses responsible for direct patient care who provide a link between clinical practice and the Antibiotic Committee.
- Manger(s) that will ensure the resources are available for implementation of the antibiotic policy.
- Reciprocal Membership between the Infection Control Committee and the Drugs Committee should be ensured

Guidelines

The guidelines should

Be drawn up after wide consultation and agreement in the hospital be simple, clear and short, and ideally published in a booklet small enough to be carried in a pocket be provided to all newly appointed doctors and nurses and readily available in the hospital, for example, available on wards contain guidance on antibiotic prophylaxis (e.g. in surgery with details of timing, route, dosage and frequency) contain guidance on the choice of antibiotics for empirical and targeted therapy of major infections indicate first and second line therapy for common infections (might limit the use of certain second line drugs to consultant prescription only)

GOOD PRACTICES FOR RATIONAL ANTIBIOTIC USE

- Consider whether or not the patient actually requires an antibiotic.
- Avoid treating colonized patients who are not actually infected.
- In general do not change antibiotic therapy if the clinical condition is improving.
- If there is no clinical response within 72 hours, the clinical diagnosis, the choice of antibiotic and/or the possibility of a secondary infection should be reconsidered.
- Give the antibiotic for the minimum length of time that is effective.
- Review the duration of antibiotic therapy after 5 days.
- Consider the use of pharmacy 'stop' policies, where drugs are written up for a - specified period and are then only continued if a new prescription is issued.
- For surgical prophylaxis start the antibiotic with the induction of anesthesia and continue for a maximum of 24 hours only.

WHO strongly recommend that governments focus control and prevention efforts in 4 main areas

- Surveillance for antibiotic resistance
- rational antibiotic use, including education of healthcare workers and the public in the appropriate use of antibiotics;

- introducing or enforcing legislation related to stopping the selling of antibiotics without prescription; and
- Strict adherence to infection prevention and control measures, including the use of hand-washing measures, particularly in healthcare facilities.

The WHO Global Strategy identifies 68 prioritized recommendations, for implementation targeted the following groups:

- Patients and the general community
- Prescribers and dispensers
- Hospitals
- Antimicrobials use in food-producing animals
- National governments and health systems
- Industry and research group
- International organizations

Materials

This study is retrospective study to the culture and susceptibility test that done in the laboratory of Al-Sadr hospital during year 2012, depending on VITEK 2 system which is an automated microbiology system utilizing growth-based technology. A culture with no growth of bacteria is considered to be (negative culture) ,while a culture with identified bacteria is called (a positive culture). If the culture is a positive, the patient report will supplied with details about type of pathogen and the different type of antibiotics and if the pathogen is sensitive (S)or resistant (R)to that antibiotic accompanied with the minimum inhibitory concentration (MIC) for each antibiotic During this period about 2664 C&S tests for all types of infection this includes (1033 for Urine), (790 t for blood), (250 ts for EAR)and (591ts for sputum)

RESULTS AND DISCUSSION

The antibiotics abuse and misuse in our hospital leads to increase the resistance to antibiotics resistance especially to ampicillin-cloxacillin combination (Ampiclox) and 3rd generation cephalosporins.

According to the hospital records about 95% of patients are given Ampiclox alone or in combination with ceftriaxone or cefotaxime as prophylactic treatment for different types of diseases. In our hospital there is no clear strategy for antibiotic prescription and administration, although they sent different samples for C&S tests and results were negative for most of tests about 26% only are positive for all patients (inpatients and patients in ambulatory ward) and

about 15% of inpatients C&S tests (table: 1), they continue to administer prophylactic systemic antibiotics to most patients.

Table 1: Show Different Types of Culture and Sensitivity Tests and Percentage of Positive Tests (Presence or Growth of Bacterial) For Inpatient Only, It Is Clear That Most of Tests Show No Growth Of Bacteria.

Test type	No. of cultures	Positive	% of positive
Urine culture	375	85	22.6%
Blood culture	642	90	14%
Sputum culture	307	5	3.45%
Ear swab	2	2	100%
All tests	1474	217	14.7%

In our study, we tried to put a guideline for most susceptible bacteria for each type of infection and drug of choice for the treatment of each bacterium according to laboratory tests to overcome the irrational use of antibiotics. Thus, for urinary tract infection, we notice that *Escherichia coli* is caused about 60%, while *Klebsiella pneumonia* is caused only 13%, and *P. mirabilis*, *p. aeruginosa* and *staph. Ssp* caused 9%, 4% and 3% respectively (table:2)

Table 2: Show Types of microorganisms in urine culture

Type of M .O.	%
<i>E. coli</i>	60%
<i>K. Pneumonia</i>	13%
<i>Prot. Mirabilis</i>	9%
<i>Pseud. aeruginosa</i>	4%
<i>Staph. Ssp.</i>	3%
<i>Leclerciaadecarboxylate</i>	2%
Others	9%

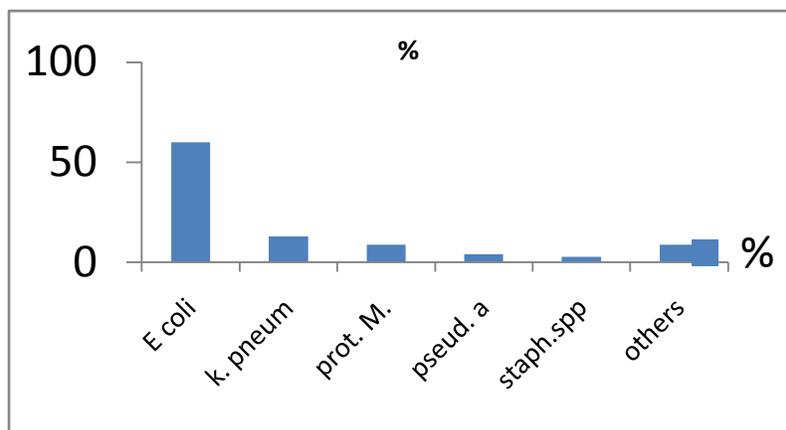


Figure 3: Show The Types of Microorganisms Causes UTI According To Culture And Sensitivity Tests

While for blood bacterial infection, we find that staphylococcus spp caused about 56% of positive C&S tests while E. coli and K. pneumonia represent 10.5% for each. (Table 3)

Table 3: Show Types Of Microorganisms Cause Septicemia According To Culture And Sensitivity Tests In Our Hospital

Type of M.o.	%
Staph. spp	56%
E .coli	10.5%
k. pneumonia	10.5%
Pasteurella. r	4.8%
Acinetobacterbaumannii	4%
Salmonella typhi	3.2%
Others	11%

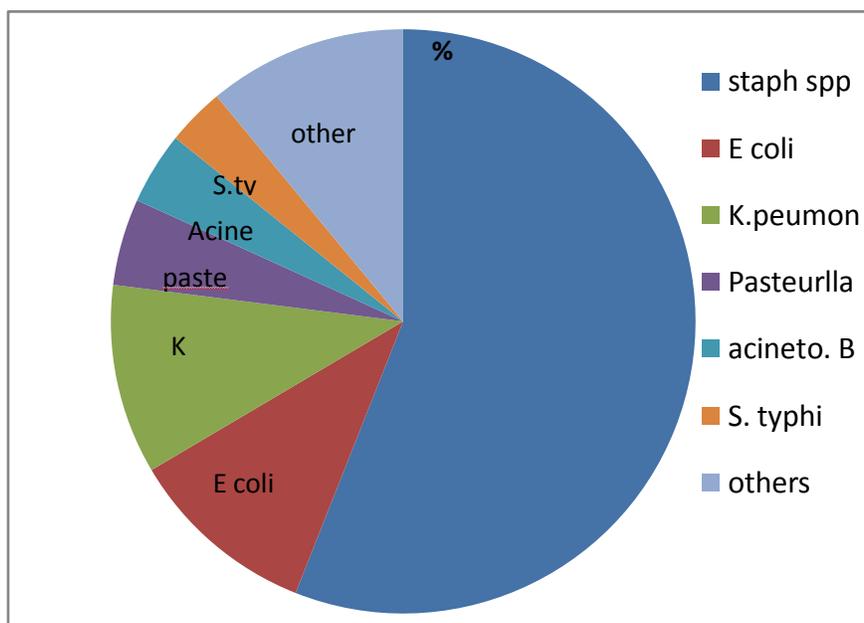


Figure: 4 show that most of ear infections caused by p. Aeruginosa

For ear infections 38% of infections are caused by pseudomonas aeruginosa, while E.coli caused only 9% (see table 4)

Table 4: Types of Bacteria Cause Ear Infection According To C&S Tests In Our Hospital

Type of M.O.	%
Pseudomonas aeruginosa	38%
Staph. spp	26%
Proteus mirabilis	12%
Klebsiella pneumonia	8%
E coli	6.5%
others	9.5%

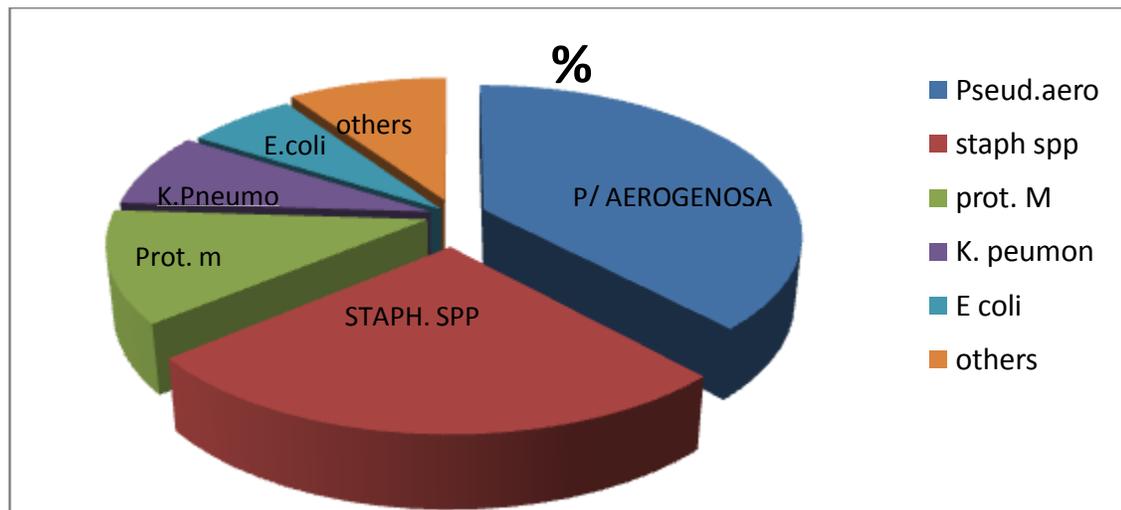


Figure: 5: The Percentage of each bacteria cause ear bacterial infection show that p. Aeruginosa caused most of them according to C&S tests

ANTIBIOTIC SENSITIVITY

During this study, we find that pseudomonas aeruginosa is sensitive in 80% to Amikacin, while it only 8% is sensitive to Augmentin (ampicillin+clavulanic acid) and 100% resistant to Ampicillin (Table: 5)

Table 5: P. Aeruginosa and its Sensitivity to Different Antibiotics According to C&S tests in our hospital

Antibiotic	Sensitivity%
Amikacin	80 %
Imipenem (tienam)	69%
Meropenem	68%
cipro	66%
Gentamicin	53%
ceftriaxone	11%
Cefotaxime	9%
Augmentin	8%
Ampicillin	0.0%

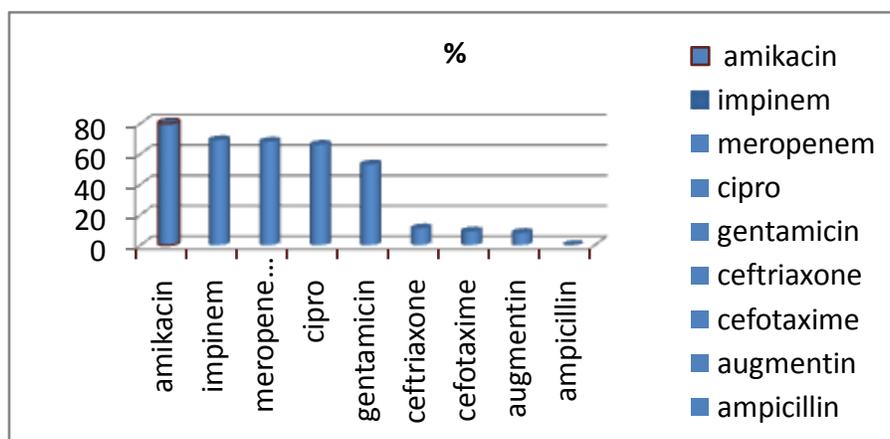


Figure 6 : The percentage of sensitivity and resistance of *P. Aeruginosa* to different antibiotics. (it is resistant to ampicillin is 100%)

While 72% of *K. pneumonia* is sensitive to each of Imipenem and Amikacin and 69% is sensitive to ciprofloxacin and also 100% was resistant to Ampicillin (table: 6)

Table 6: *K. Pneumonia* and its sensitivity to different antibiotics according to C&S tests in our hospital

Antibiotics	% of sensitivity
Imipenem	72%
Amikacin	72%
Cipro	69%
Gentamicin	59%
Tetracycline	55%
Cefepime	50%
Augmentin	40%
Cefotaxime	36%
Ceftriaxone	17%
Ampicillin	0.0%

P. mirabilis is 100% sensitive to Imipenem and sensitive to Ampicillin and Ceftriaxone only in 36% and 22% respectively (table: 7)

Table 7: *P Mirabilis* and its sensitivity to different antibiotics according to c&s tests

Antibiotics	Sensitivity %
Imipenem	100%
Cipro	98%
Amikacin	97%
Gentamicin	80%
Augmentin	66%
Cefepime	46%
Ceftriaxone	38%
Ampicillin	36%
Cefotaxime	22%

For E.coli ,it was 95% sensitive to Imipenem and 89% was sensitive to Amikacin and resistant in 75% and 69% to cefotaxime and ceftriaxone respectively and resistant in 92.5% to ciprofloxacin due to abuse of this antibiotics (table: 8)

Table 8: E. coli and its sensitivity to different antibiotics according to C&S tests And finally: staph. Ssp. Which were resistant in 90% to Ampicillin and in 62% resistant to ceftriaxone

Antibiotics	Sensitivity %
Imipenem	95%
Amikacin	89%
Gentamicin	56%
Cefepime	50%
Augmentin	46%
Ceftriaxone	31%
Cefotaxime	25%
Ampicillin	15%
Cipro	7.5%

Table: 9 Staph. species and its sensitivity to different antibiotics according to C&S tests in our hospital (only 10% are sensitive to ampicillin)

Antibiotics	Sensitivity %
Vancomycin	93%
Imipenem	89%
Cloxacillin	72%
Gentamicin	70 %
Cipro	60 %
Erythromycin	60%
Clindamycin	54%
Ceftriaxone	38%
Ampicillin	10 %

Penicillin sensitivity in al-Sadr hospital

While from all C&S tests (2664) during year 2012 there were only 69 cases are sensitive to Ampicillin and about only 0.4% of inpatients C%S tests are sensitive to Ampicillin while physicians continue to prescribe Ampicillin to most of patients as prophylactic treatment .it is really a catastrophe.(figure :6)

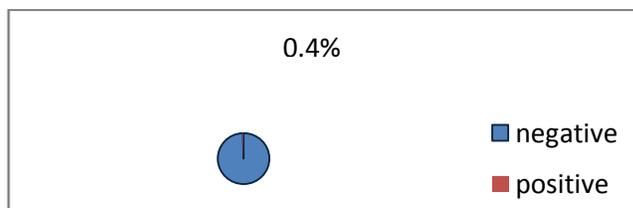


Figure 7: This figure represents the sensitivity of all microorganisms to penicillin's for inpatients, only 0.4 % of tests are sensitive to Ampicillin

Cost of irrational antibiotics use

The cost of antibiotics during 2012 is according to the pharmacy records. While the cost of antibiotics during in which the admission during 2011 is 35,892 which is similar to that in our hospital,

These results showed that the abuse and misuse and antibiotics in our hospital led to increase in resistance of bacteria to all antibiotics especially ampicillin and ceftriaxone, so we feel that we lose the effectiveness of most antibiotics which led to increase the cost of antibiotics which was more than 2 million dollars (USD) (about **2,050,924\$**) which is very high when compared with other hospitals in neighboring countries, 2011 in hospital of Ataturk University Medical School in Erzurum Turkey which is the largest hospital in eastern Anatolian Region of Turkey, the cost is about **1,077,000\$**. So that irrational use of antibiotics led to increase its resistance and cost of treatment.

CONCLUSION

Penicillin and most of cephalosporins are no longer a drug of choice for most of bacterial infections including staphylococcus bacterial infections in Iraq due to excessive use of them. Most of the medical problems that were thought to be caused by bacterial infections, they are not. Only about 26% of them are caused by bacteria. There is no critical need for antimicrobial prophylaxis for most of cases.

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