Ministry of higher education
And scientific research

University of Al- Qadisiya
College of Pharmacy

Awareness of Bacterial Resistance Among Iraqi Pharmacist

A research submitted to the college of pharmacy of the requirements for the degree of B.se of pharmacy.

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بسم الله الرحمن الرحيم

{ يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ }

صدق الله العلي العظيم

سورة المجادلة ، آية ١١

الأهداء

اهدي هذا البحث العلمي إلى من جرع الكأس فارغاً ليسقيني قطرة حب
إلى من كلّت أنامله ليقدم لنا لحظة سعادة
إلى من حصد الأشواك عن دربي ليمهد لي طريق العلم
إلى القلب الكبير (والدي العزيز)

إلى من أرضعتني الحب والحنان
إلى رمز الحب وبلسم الشفاء
إلى القلب الناصع بالبياض (والدتي العزيزة)

إلى القلوب الطاهرة الرقيقة والنفوس البريئة إلى رياحين حياتي (أخوتي و أخواتي)

الآن تفتح الأشرعة وترفع المرساة لتنطلق السفينة في عرض بحر واسع مظلم هو بحر الحياة وفي هذه الظلمة لا يضيء إلا قنديل الذكريات ذكريات الأخوة البعيدة إلى الذين أحببتهم وأحبوني(أصدقائي)

Contents:

Abstract:

Objective: To assess the level of pharmacist's awareness of bacterial resistance and characterize the most common resistant bacterial species, the factors contributing to the development of such resistance, and the possible measures to limit the increasing rate of resistance to current antibacterial therapies.

Method: A questionnaire was administered to 125 pharmacists in their work places weather in community pharmacies or hospitals pharmacy. Results: Our results indicate that most of the responding pharmacists considered methicillin- resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant *enterobacteraceae* (VRE) the most frequently encountered resistant bacterial species. Most Pharmacists reported prolonged hospitalization as a factor likely to contribute to the increased incidence of bacterial resistance. About 58.88% of pharmacists indicated the use of antibiotics without prescription as a significant reason for the development of bacterial resistance. Most pharmacists reported that appropriate infection control is the most important measure to reduce bacterial resistance. (54.21%) of Pharmacists recognized better adherence to the infection control guidelines as somewhat likely most important factor that could reduce the risk of bacterial resistance.

Conclusion: The findings of this study indicate a varying level of awareness of bacterial resistance among the pharmacists. Thus, serious efforts are still needed to develop and implement strategies to decrease the future risk of bacterial resistance to antibiotics.

Certification

This is certify that this research was prepared under my supervision at the University of Al-Qadisiya, College of Pharmacy, as a partial requirements for the degree of Bachelor in pharmacy.

Signature:

Advisor's Name: Prof.D Mohsen Alrodhan

Date: / /2017

Introduction

The initiation of antibiotic use in the form of indiscriminate prescribing and dispensing has led to an upsurge in the resistance gene in the commensal flora in hospitals, in communities, and in the environment (Alvan ,et al ,2011) .Imprudent use of antibiotics is a fundamental factor for an upsurge in the prevalence of antimicrobial resistance (Shehadeh et al ,2012 / Kumar et al ,2012) .Factors such as patients' demands, doctors' personal experiences, lack of culture and sensitivity results leading to uncertain diagnosis, sales of antibiotics without prescription, and pharmaceutical promotional tactics are some of the most common contributors towards antibiotic resistance (Srinivasan , et al, 2004 / Lim, et al , 1993)The report of Malaysian Statistics on Medicine 2007 indicated anti-infective agents as the

most commonly prescribed therapeutic category in Malaysia with a 7% increase in consumption of antiinfectives from 2006 to 2007. Systemic use of antibacterial drugs added the highest increase, accounting for 89% of the total increase. This is not unexpected, as antibacterial drugs (124 drugs) constitute the largest group of anti-infective drugs. Pencillins were the chief therapeutic category consumed in 2007, with macrolides and tetracyclines trailing behind penicillins. Ampicillin, amoxicillin, and bacampicillin were extensively used in both public and private sectors for initiating the empiric treatment of upper respiratory tract infections (URTIs), urinary tract infections (UTIs), and mild community-acquired pneumonia (CAP) .It is interesting to note that, as per National Antimicrobial Resistance Surveillance data, high resistance of Gram-negative bacteria such as *Klebsiella spp*. (99%), *Enterobacter spp*. (93%), Escherichia coli (69%), Proteus spp. (48%) and *Haemophilus influenzae* (20%) was observed towards ampicillin. There is a need to analyze the use of these antibiotics as empirical therapy in the primary healthcare setting. Previously published research from Malaysia reflected on the need for creating awareness among the general public and hospital doctors about the role of antibiotics in viral infections, the aftermath of self-medication in cough and cold symptoms, and as well as compliance with guidelines on antibiotic use issued by the Ministry of Health, Malaysia (Lim, et al , 1993 / Lim , Teh , 2012 / Ling, et al ,2010)Patient-focused educational outreach to change patients' mindsets is a key area to be targeted (Finch et al, 2004) Therefore, before embarking on any interventions to patients or the public, it is necessary to ascertain the understanding of future healthcare practitioners; this study is an attempt in this regard

Staphylococcus aureus bacteremia is a serious infection that leads to significant morbidity and mortality in adults and children. (Burke et al ,2009/ Mylotte / Tayara ,2013).Up to 50% of healthy adults are naturally colonized with *S. aureus*. (Noble et al ,1967/1986). There are two major types of infection sources: community acquired and hospital infections. This bacterium causes therapeutic problems due to infections with strains which are resistant to many antibiotics and particularly resistant to methicillin: methicillinresistant *Staphylococcus aureus*. (Ito, et al ,2007) MRSA strains were discovered in 1961 (Sasidharan et al, 2011). Methicillinresistant *Staphylococcus aureus* (MRSA) is the most commonly identified antimicrobial resistant pathogen in hospitals in many parts of the world. In Europe, the proportion of methicillin resistance in strains of *Staphylococcus aureus* (S. aureus) isolates in infected patients varied in 2011 from less than 0.5% to more than 50%, with a pooled mean rate of around 17%. This bacterium is very adaptable and able to cross all host defense system barriers due to its wide spectrum of virulence factors. (Plata ,et al ,2009) Colonization with *Staphylococcus aureus* has a well-recognized association with development of infection, including surgical site and blood stream infections. (Perl, et al ,2002/ pujol et al ,1996).It is known that individuals can be colonized with *S. aureus* in sites other than the nose, including the throat, axilla, groin and rectum and it is thought that these non-nasal sites might be important in the pathogenesis of infection.(Peña, et al , 2004).The anterior nares are the main reservoir of MRSA, although other body sites are frequently colonized, such as the hands, skin, axillae, and intestinal tract. Colonized individuals are generally asymptomatic and three types of MRSA carrier status can be distinguished: noncarriers, persistent carriers, who are chronically colonized with the same strain, and intermittent carriers, who are colonized with varying strains for short time. (Acton, et al,2009/ Albrich, Harbarth, 2008). This pathogen also poses a risk of device-related infections, e.g., related to the use of intravascular catheters, propylene nets ventriculoperitoneal shunts, pacemakers, and orthopedic implants. (Priest, Peacock ,2005/ Collins, Hampton ,2005/ Fowler ,et al ,2005/ Nowakowska, et al ,2007/ Abele-Horn, et al, 2000/ Fadda, et al,2005/ Seifert, et al,2003). The most important mode of MRSA transmission is through contamination of the hands. (Cimolai ,2008) An alternative mechanism of transmission is airborne dispersal of staphylococci in association with an upper respiratory tract infection. (Sherertz et al,1996). *S. aureus* can be both a commensal and a dangerous pathogen causing severe infections—skin abscesses, *endocarditis*, *pneumonia*, osteomyelitis—even leading to toxic shock syndrome. S. aureus infection is a major cause of skin, soft tissue, respiratory, bone, joint, and endovascular disorders. Staphylococcus aureus is gradually acquiring resistance to previously effective antimicrobial agents. Therefore, since the 1960s, infections caused by this bacterium have become particularly difficult to treat. (Lowy, et al,1998). Methicillin resistant *Staphylococcus aureus* (MRSA) has emerged as one of the commonest causes of hospital acquired infections worldwide. The infection caused by MRSA increases the length of hospital stay and it is also responsible for raising health care expenses and morbidity. Resistance to all antibiotics which are available for use against Staphylococcus aureus has been reported. In a study done by K. Rajaduraipandi, 63.2% MRSA were found to be resistant to gentamycin, cotrimoxazole, cephalexin, erythromycin and cephotaxim. (Rajaduraipandi, et al,2006). Ciprofloxacin usage has already been known to be associated with selection of MRSA (Sharma , Ahmed ,2010) .

Aim of study

To assess the level of pharmacist's awareness of bacterial resistance and characterize the most common resistant bacterial species, the factors contributing to the development of such resistance, and the possible measures to limit the increasing rate of resistance to current antibacterial therapies.

Literature review

Each time you take an antibiotic, bacteria are killed. When an antibiotic is taken unnecessarily or improperly, some bacteria can survive. The surviving bacteria develop ways to become stronger and drug-resistant. Resistant bacteria can transfer this strength to other more dangerous bacteria. There are three ways you can get an antibiotic resistant infection: - You can develop antibiotic resistant infections when you take an antibiotic. Bacteria that have been exposed to the antibiotic but have developed ways to fight them survive. They then can multiply and begin to cause symptoms. You can also transmit resistant bacteria to others and they too may become ill. You can catch antibiotic resistant infections from people or objects around you that are infected with resistant bacteria. Resistant bacteria are frequently found among people in hospitals, nursing homes or day care centers. Not properly washing hands can increase your risk of catching all kinds of infections. You can develop an antibiotic resistant infection when the bacteria inside your body exchange, share or copy genes that allow them to resist antibiotic treatment. (Peterson ,2012).

And for more details about the history of antimicrobial resistance, looking back on the history of human diseases, infectious diseases have accounted for a very large proportion of diseases as a whole. It was not until the latter half of the 19th century that microorganisms were found to be responsible for a variety of infectious diseases that had been plaguing humanity from ancient days. Accordingly, chemotherapy aimed at the causative organisms was developed as the main therapeutic strategy. The first antimicrobial agent in the world was salvarsan, a remedy for syphilis that was synthesized by Ehrlich in 1910. In 1935, sulfonamides were developed by Domagk and other researchers. These drugs were synthetic compounds and had limitations in terms of safety and efficacy. In 1928, Fleming discovered penicillin. He found that the growth of Staphylococcus aureus was inhibited in a zone surrounding a contaminated blue mold (a fungus from the Penicillium genus) in culture dishes, leading to the finding that a microorganism would produce substances that could inhibit the growth of other microorganisms (Hashimoto, 2000). The antibiotic was named penicillin, and it came into clinical use in the 1940s. Penicillin, which is an outstanding agent in terms of safety and efficacy, led in the era of antimicrobial chemotherapy by saving the lives of many wounded solders during World War II. During the subsequent two decades, new classes of antimicrobial agents were developed one after another, leading to a golden age of antimicrobial chemotherapy. In 1944, streptomycin, an aminoglycoside antibiotic, was obtained from the soil bacterium Streptomyces griseus. Thereafter, chloramphenicol, tetracycline, macrolide, and glycopeptide (e.g., vancomycin) were discovered from soil bacteria (Hashimoto, 2000). The synthesized antimicrobial agent nalidixic acid, a quinolone antimicrobial drug, was obtained in 1962. Improvements in each class of antimicrobial agents continued to achieve a broader antimicrobial spectrum and higher antimicrobial activity. lactam antibiotics will be described as an example. The -lactam antibiotics include penicillins, cephems, carbapenems, and monobactams. Penicillins were originally effective for Grampositive organisms such as S.aureus. Later, to address penicillin-resistant S.aureus which produces the penicillin-hydrolysing enzyme penicillinase, methicillin was developed. On the other hand, attempts to expand the antimicrobial spectrum yielded ampicillin, which is also effective for Gram-negative Enterobacteriaceae, and piperacillin, which is effective even for Pseudomonas aeruginosa. Cephems were developed in the 1960s, and came into widespread use. Cephems are classified into several generations according to their antimicrobial spectra. First-generation cephems (cefazolin, etc.) are effective only for Gram-positive organisms and Escherichia coli, although their antimicrobial activity against these organisms is potent (Powers ,2004). Second-generation cephems (cefotiam, etc.) have an extended antimicrobial spectrum that covers not only Gram-positive but also Gramnegative organisms including other Enterobacteriaceae. Third-generation cephems (ceftazidime, cefotaxime, etc.) have higher efficacy for Gramnegative organisms, and some drugs of this generation are also effective for P. aeruginosa, although the antimicrobial activity against Grampositive organisms is generally lower than that of the first generation. Carbapenem is an antibiotic class including panipenem, imipenem, and meropenem. These drugs are effective not only for Gram-positive and Gram-negative bacteria but also anaerobes, and their antimicrobial activity is strong. The monobactam antibiotic aztreonam exerts an antimicrobial effect only on Gram-negative bacteria. Continuing improvements have been made for antimicrobial agents in various aspects in addition to the antimicrobial spectrum and activity. The drugs have been developed to achieve better pharmacodynamics including the absorption of oral drugs, concentration in the blood, and distribution to the inflammatory focus. In addition, as antimicrobial chemotherapy has been established and matured, more importance has been attached to the drug safety. Antimicrobial agents that are associated with serious side effects have been replaced by other safer drugs. Quinolone antimicrobials represent an example of drugs with improved pharmacodynamics and safety . Nalidixic acid, the first drug of this class, was active only against Gram-negative bacteria, and its use was limited to urinary tract infections because it achieves only low blood concentrations and poor tissue distribution, and was metabolized rapidly in the human body. In contrast, norfloxacin, which came to market in 1984, maintains a stable metabolic state and exhibits good tissue distribution. Its antimicrobial spectrum is extensive, covering both Grampositive and Gram-negative bacteria including P. aeruginosa (Powers ,2004). Quinolone antimicrobials developed after norfloxacin have been called new quinolones, and they have still been key drugs. Levofloxacin is the S- (-) enantiomer of the new quinolone ofloxacin. This enantiomer has higher antimicrobial activity than that of the other R- (+) enantiomer of ofloxacin, and is associated with weaker side effects on the central nervous system, such as restlessness and vertigo. Although a large number of companies in various countries have competed in the development of newer antimicrobial agents, the number of brand new drugs has been remarkably decreasing in recent years, with few antimicrobial agents of new classes becoming available. In contrast, infectious diseases continue to attack human beings as emerging and re-emerging infectious diseases, opportunistic infectious diseases, and infection with drug-resistant microorganisms that will be discussed in the next section. Effective utilization of the current limited options is much more important under the dearth of new drugs on the market. (Powers ,2004).

The four main mechanisms by which microorganisms exhibit resistance to antimicrobials are: Drug inactivation or modification: for example, enzymatic deactivation of *penicillin G* in some penicillin-resistant bacteria through the production of β-lactamases. Most commonly, the protective enzymes produced by the bacterial cell will add an acetyl or phosphate group to a specific site on the antibiotic, which will reduce its ability to bind to the bacterial ribosomes and disrupt protein synthesis. (Criswell, Daniel.2014). Alteration of target- or binding site: for example, alteration of PBP—the binding target site of penicillins—in MRSA and other penicillin-resistant bacteria. Another protective mechanism found among bacterial species is ribosomal protection proteins. These proteins protect the bacterial cell from antibiotics that target the cell's ribosomes to inhibit protein synthesis. The mechanism involves the binding of the ribosomal protection proteins to the ribosomes of the bacterial cell, which in turn changes its conformational shape. This allows the ribosomes to continue synthesizing proteins essential to the cell while preventing antibiotics from binding to the ribosome to inhibit protein synthesis. (Criswell, Daniel.2014). Alteration of metabolic pathway: for example, some sulfonamide-resistant bacteria do not require para-aminobenzoic acid (PABA), an important precursor for the synthesis of folic acid and nucleic acids in bacteria inhibited by sulfonamides, instead, like mammalian cells, they turn to using preformed folic acid. (Criswell, Daniel ,2014). Reduced drug accumulation: by decreasing drug permeability or increasing active efflux (pumping out) of the drugs across the cell surface. (*Nikaido .2009*). These pumps within the cellular membrane of certain bacterial species are used to pump antibiotics out of the cell before they are able to do any damage. They are often activated by a specific substrate associated with an antibiotic. (Aminov, Mackie.2007) as in fluoroquinolone resistance. (*Morita et al.1998*).

Methodology

This was a cross-sectional study that used a prevalidated, pre-tested study instrument. As this study was conducted to investigate the understanding of antibiotic resistance among pharmacists, all pharmacists were contacted. A total of 50 questionnaires were distributed to pharmacists in their pharmacy with the help of my colleague in the study, and 75 questionnaires were distributed to pharmacists whose work in the hospitals. The questionnaires were completed by the pharmacists and collected on the next week. the data were collected in October 2016. Of 125 questionnaires distributed, only 110 responses were successfully collected back.

The study instrument was a questionnaire which was formed on the basis of extensive literature search (Shehadeh,2012 /kumar,2011/ling,2010/ghadeer,2012/wright,2004). The pilot data was entered in SPSS version 17 to evaluate the reliability coefficient. Reliability coefficient was found to be 0.85. Data was analyzed using SPSS version 24. Descriptive and inferential statistics were applied.

Study tool: design and development of questionnaire

The questionnaire contained 32 questions. It investigated five main areas:

- The participant's demographic information (5 questions): age, gender, education, number of years sent in pharmacy practice, currently working at hospital or community pharmacy.
- Pharmacists knowledge of most frequently bacterial species in medical: MRSA, VRE, ESBL, *aeruginosa B., A.baumannii.*
- Most common factors contributing bacterial resistance: Awareness of antibiotics action, indications, causes and consequences of antimicrobial resistance (10 questions).
- Strategies to control bacterial resistance: contain (10 questions)
- Pharmacists opinions on the future risk of bacterial resistance: contain (2 questions), bacterial resistance will become worse if current practices do not change? Will bacterial resistance be controlled?

***Statistical analysis**

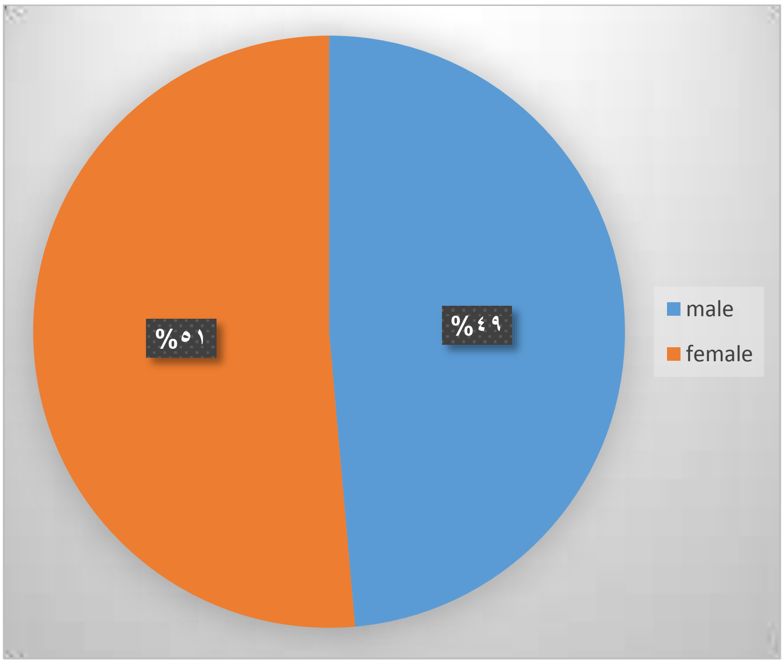
We used SPSS 24.0 to analyze data, using T-test method at level 0.05. and the data found in the appendix (1)

Results

Sample size and demography

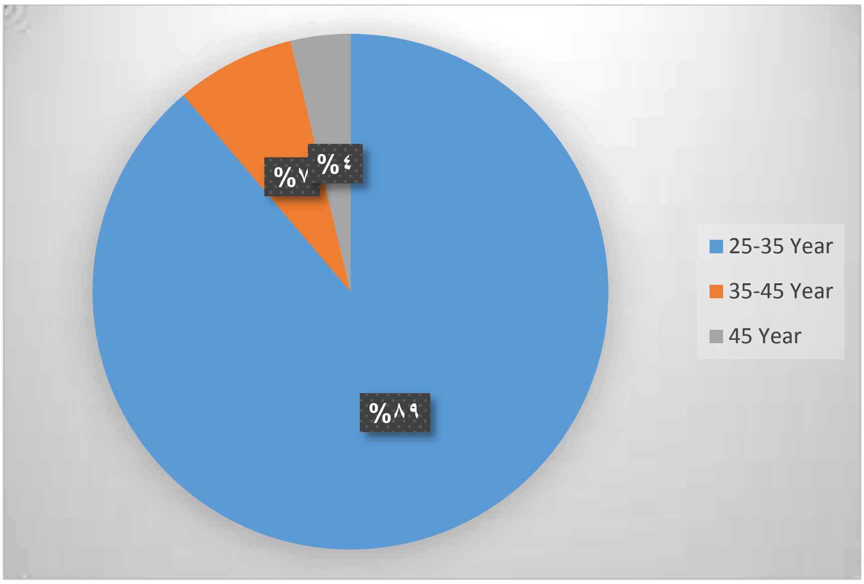
The participants who agreed to answer the questionnaire in this study were 125 pharmacists, there was a response rate of 85.6%. Of 125 questionnaires distributed, only 110 responses were successfully collected back. Three cases were excluded because they were not answered by the pharmacists.

The results were in relate to pharmacist gender, the proportion of female was 51% while male equal to 49%. (Figure 1)



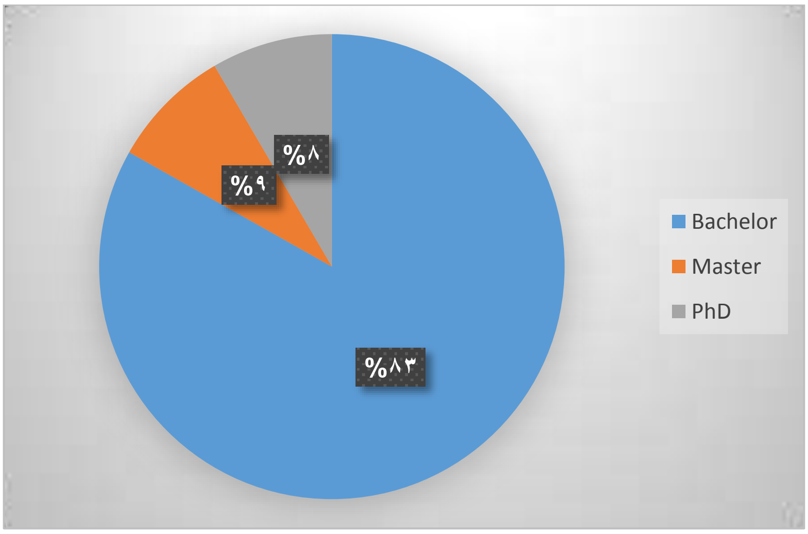
(figure 1) explain the proportion of male and female.

While the results were in relate to pharmacist years of work were 89% of the samples in which the age was between 25-35 year, 7% between 35-45 year, and 4% their age was 45 years and more. (Figure 2)



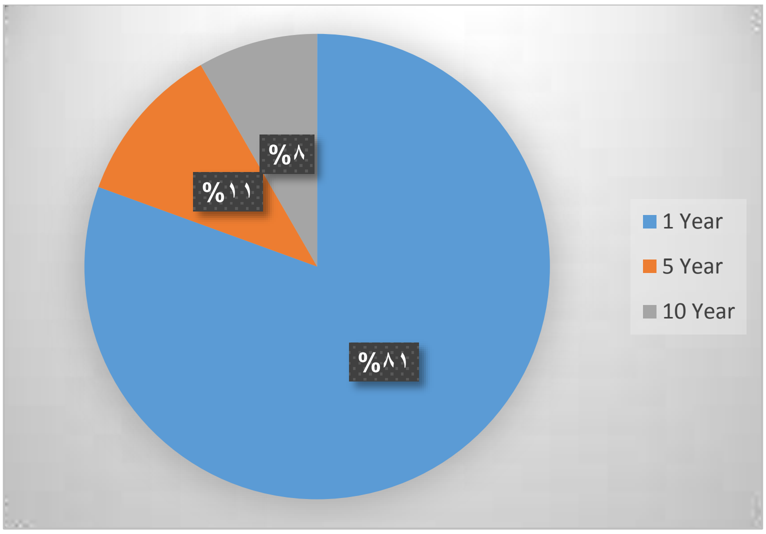
(Figure 2) explain pharmacist's age group

The results in relate to pharmacist education were ,83.1% bachelor's degree ,8.4% master degree, and 8.4% Ph.D. degree. (Figure 3)



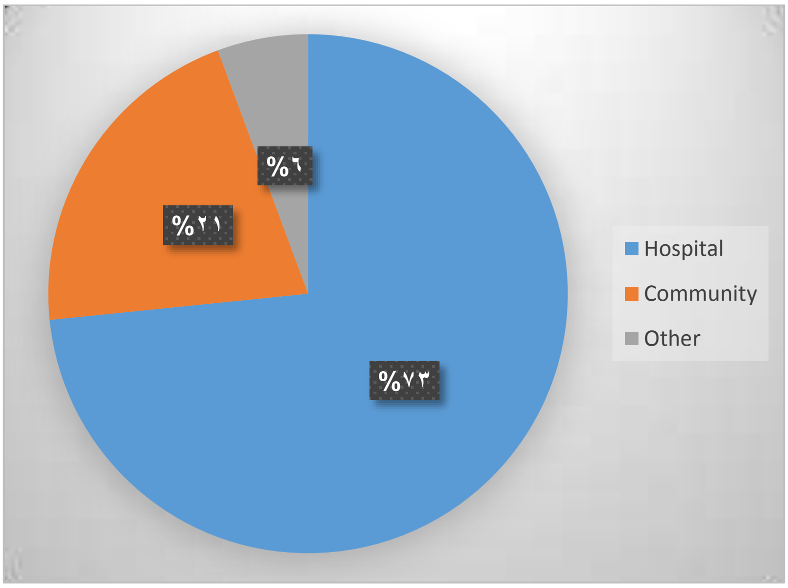
(figure 3) explain pharmacist's education

The results were in relate to pharmacist work were 81% of the samples in which the pharmacists work for 1-5 years, 11% work for 5-10 years, and 8% work for more than 10 years. (Figure 4)



(Figure 4) explain pharmacist's years work

The results were in relate to pharmacist work place, 73% working in the hospitals, 21% working in community pharmacy, and 6% working in other places. (Figure 5)



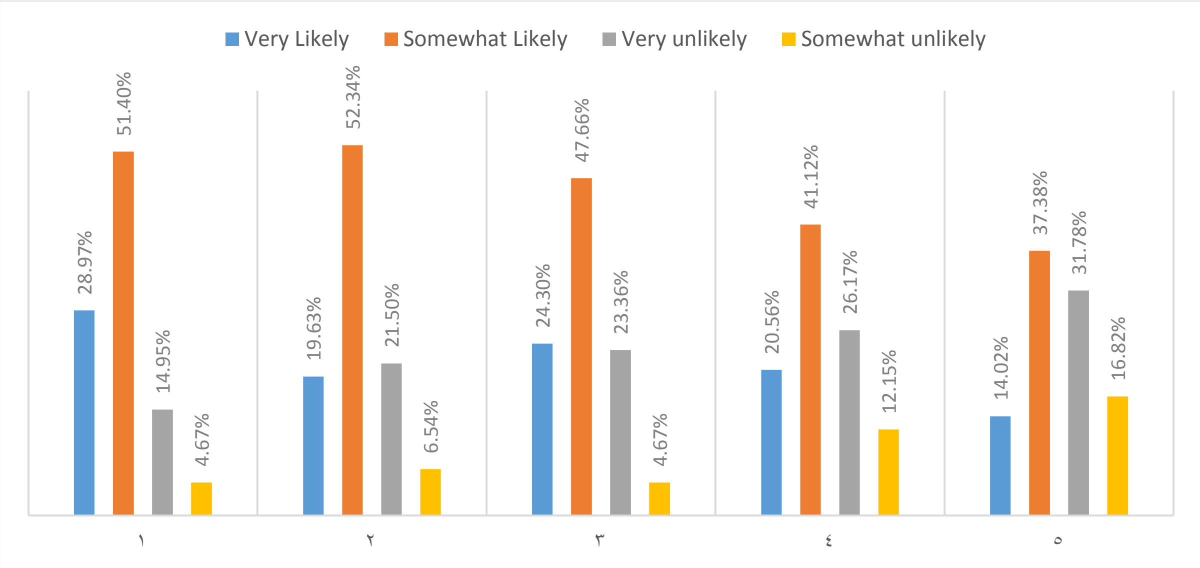
(figure 5) explain pharmacist work place

The results of pharmacist's knowledge of most frequently bacterial species in medical practice were

For the methicillin resistance *staph. Aurus* MARSA, the answers were 31(28.97%), 55(51.40%), 16(14.95%), 5 (4.67%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively . The p value was 0.09 and so it not significant value.

For vancomycin resistance *enterobacteracae* VRE, the answers were 21(19.63%), 56(52.34%), 23(21.50%), 7(6.54%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.082 and so it not significant value.

For extended release B lactamase producing gram negative *bacilli* ESBL, the answers were 26(24.30%), 51(47.66%), 25(23.36%), 5(4.67%) , very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.066 and so it not significant value.For aeruginosa B., the answers were 22(20.56%), 44(41.12%) , 28(26.17%) , 13(12.15%) ,very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.o26 and so it significant value.For *A. baumannii*, the answers were15(14.02%), 40(37.38%), 34(31.78%), 18(16.82%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.o22 and so it significant value. (figure 6)



(figure 6) Pharmacists knowledge of most frequently bacterial species in medical practice

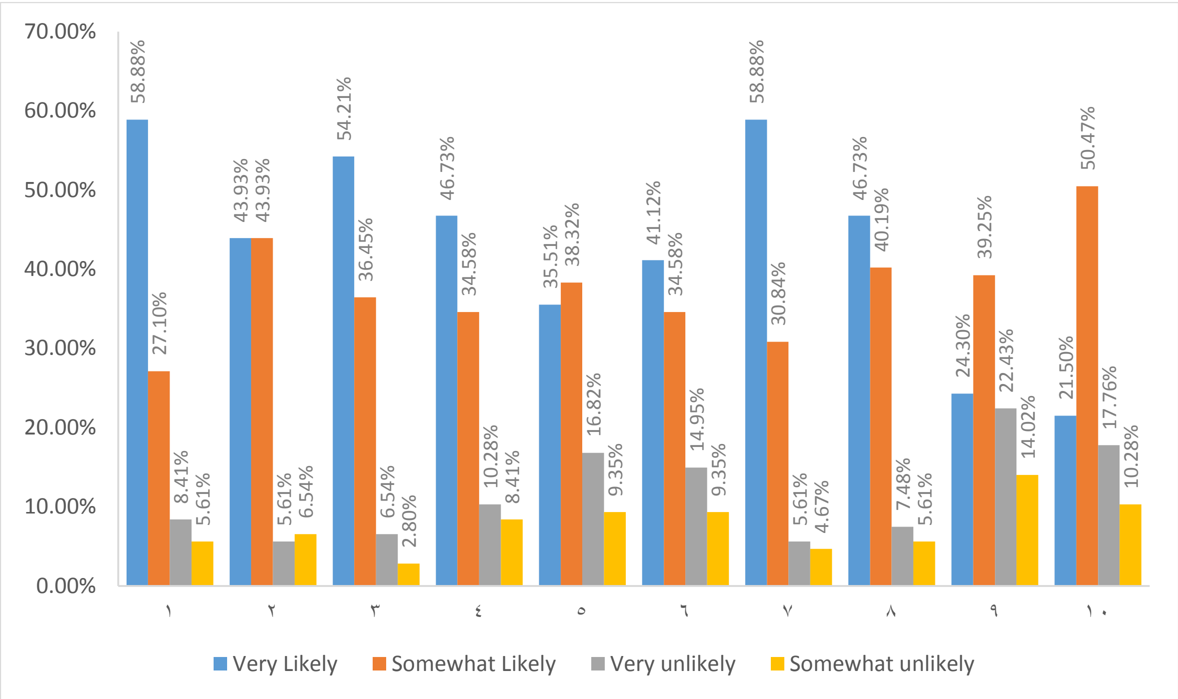
The results of Most common factors contributing bacterial resistance were

Prolonged hospitalization, the answers were 63(58.88%), 29(27.10%), 9(8.41%), 6(5.61%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.135 and so it not significant value.Inappropriate infection control practice, the answers were 47(43.93%), 47(43.93%), 6(5.61%), 7(6.54%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.107 and so it not significant value. Improper antibiotic prescription, the answers were 58(54.21%), 39(36.45%), 7(6.54%), 3(2.80%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.136 and so it not significant value.

Extensive use of newer generation of antibiotic, the answers were 50(46.73%), 37(34.58%), 11(10.28%), 9(8.41%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.076 and so it not significant value.

High rate of patients transfer between hospital units, the answers were 38(35.51%), 41(38.32%), 18(16.82%), 10(9.35%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.039 and so it significant value.

Patients noncompliance, the answers were 44(41.12%), 37(34.58%), 16(14.95%), 10(9.35%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.o47 and so it significant value.Use antibiotic without medical prescription, the answers were 63(58.88%), 33(30.84%), 6(5.61%), 5(4.67%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.147 and so it not significant value.Prescribing antibiotic where no blood culture performed, the answers were 50(46.73%), 43(40.19%), 8(7.48%), 6(5.61%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.103 and so it not significant value.Food of animal source, the answers were 26(24.30%), 42(39.25%), 24(22.43%), 15(14.02%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.o18 and so it significant value. Instruments increase use of medical, the answers were 23(21.50%), 54(50.47%), 19(17.76%), 11(10.28%) ,very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.066 and so it not significant value. (figure 7)



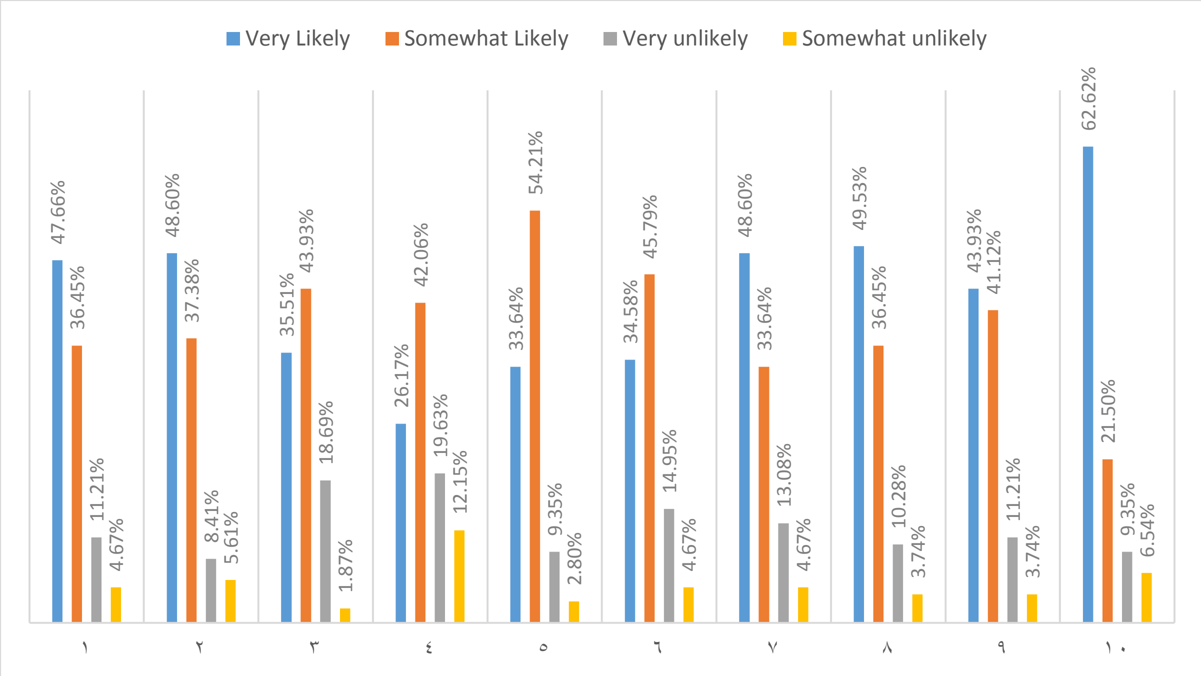
(figure 7) Most common factors contributing bacterial resistance

The results of Strategies to control bacterial resistant were

Better hygiene practice, the answers were 51(47.66%), 39(36.45%), 12(11.21%), 5(4.67%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively . The p value was 0.092 and so it not significant value. Appropriate infection control practice, the answers were 52(48.60%), 40(37.38%), 9(8.41%), 6(5.61%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.101 and so it not significant value.Reducing hospital stay, the answers were 38(35.51%), 47(43.93%), 20(18.69%), 2(1.87%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.075 and so it not significant value.Limiting use of medical instrument, the answers were 28(26.17%), 45(42.06%), 21(19.63%), 13(12.15%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.030 and so it significant value.Better adherence to infection control guidelines, the answers were 36(33.64%), 58(54.21%), 10(9.35%), 3(2.80%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.124 and so it not significant value.Hospital internal restriction, the answers were 37(34.58%), 49(45.79%), 16(14.95%), 5(4.67%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.075 and so it not significant value.Better antibiotic handling strategies, the answers were 52(48.60%), 36(33.64%), 14(13.08%), 5(4.67%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.087 and so it not significant value.Antibiotic cycling, the answers were 53(49.53%), 39(36.45%), 11(10.28%), 4(3.74%) , very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.104 and so it not significant value.

Education program of general public, the answers were 47(43.93%), 44(41.12%), 12(11.21%), 4(3.74%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.093 and so it not significant value.Accurate diagnosis, the answers were 67(62.62%), 23(21.50%), 10(9.35%) 7(6.54%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.150 and so it not significant value.

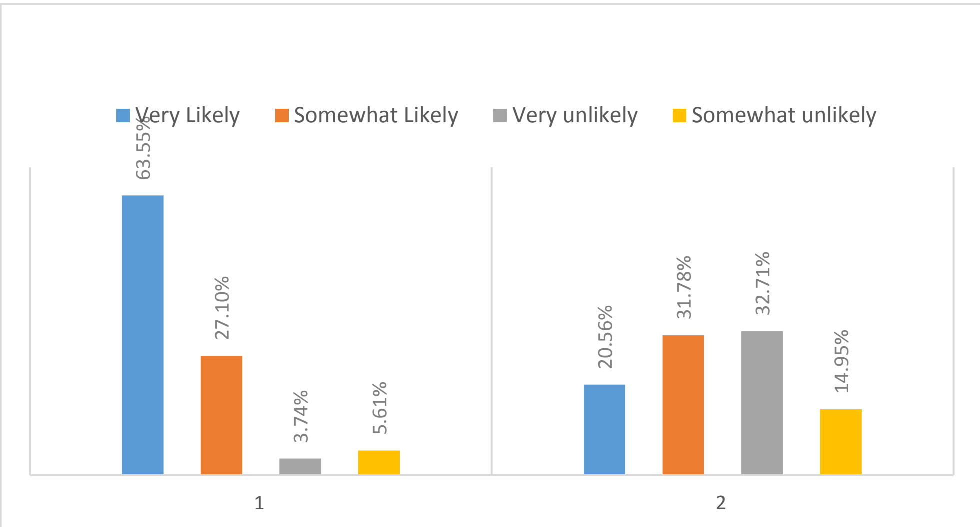
(figure 8)



(figure 8) Strategies to control bacterial resistant

The results of pharmacist’s opinions on the future risk of bacterial resistant

Bacterial resistant will become worse if current practices do not change, the answers were 68(63.55%), 29(27.10%), 4(3.74%), 6(5.61%),very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.171 and so it not significant value.Be controlled bacterial resistant will, the answers were 22(20.56%), 34(31.78%), 35(32.71%), 16(14.95%), very likely, somewhat likely, very unlikely, somewhat unlikely, Respectively. The p value was 0.010 and so it significant value. (figure 9)



(figure 9) Pharmacists opinions on the future risk of bacterial resistant

Discussion

Antimicrobial resistance is a major problem for the global health and economy all over the world (Martin et al.2004). In the developing countries, a high rate of infections usually correspondes with a development and spread of microbial resistance (Okeke et al.2005). The findings of this study revealed that most of the pharmacists in Iraq. as highly resistant bacteria ranked not only (MRSA) but also (VRE)as belonging to the most resistant microorganisms. There is association between the bacterial species listed in our questionnaire and antibiotic resistance varies considerably. The difference in the assessment between representatives of pharmacists can be attributed to individual knowledge and personal experience with such infectious agents. The Gram-positive bacteria resistant to antibiotics are a common cause of nosocomial (hospital-acquired) blood stream infections in the United States (rice lb. 2006). MRSA isolates are resistant to available β-lactam antibiotics, including penicillins and cephalosporins (Daum RS.2007). Since the late 1970s, MRSA isolates have been the reported cause of many hospital outbreaks worldwide. They can be encountered in small community hospitals, chronic care facilities, and even within the community (Cunha BA.2005) and (sulberg CO.2000).In addition, resistance to vancomycin has been acquired by the strains of *Enterococcus faecium,* thus accounting for treatment failures. At present, five types of vancomycin resistance have been reported for *Enterococci*(Amyes SG.2007) On the other hand, multidrug resistant *P. aeruginosa* strains are one of the most common Gram-negative bacilli which are the cause of nosocomial infections with a high incidence of morbidity and mortality (Elkin S, Geddes D*.2003)(* Navon-Venezia S*.2005).Acinetobacter* is another important causal agent of nosocomial infections that has been associated with many illnesses in hospitalized patients, especially in the intensive care units (ICUs) (Bergogne-Berezin E, Towner KJ*.1996).Acinetobacter* is frequently resistant to aminoglycosides, flouroqiunolones, ureidopenicilliuns, and third-generatiof cephalosporins as well as carbapenems .Many factors have been associated with the emergence and spread of antimicrobial resistance. In fact, the use of antimicrobial agent, by itself, is considered to exert a selective pressure on resistance (Okeke et al.2005). In addition, the use of antibiotics for the treatment of non-bacterial, mostly viral, infections, and the overuse of broad-spectrum antibiotics in the management of bacterial infections promotes antibiotic resistance (Austin DJ. et.al.1999) and increases the costs of health care(Huovinen P. et.al.1997). Inappropriate prescription of more expensive or second-line antibiotics in daily clinical practice is considered even more problematic (Okeke et al.2005). A past report discusses the underlying reasons for the differences in antibiotic prescription practice as applied by health care professionals. A major reason for the large-scale prescription of antibiotics is inadequate knowledge about the consequences of bacterial resistance as a worldwide problem. Secondly, it is believed that the rate of this practice increases due to the growing demand for antibiotics on the part of the patients. This results in the pharmacists softening their attitude and responding to these expectations. Thirdly, the educational aspect, which is related mainly to the professional or cultural background of the pharmacists, is thought to play a role (Cadieux G. et.al.2007). Finally, it was shown that the phrmacists who take care of a large number of patients are more likely to prescribe antibiotics when these are not appropriate (Figueiras A.et.al.2000)(rossi A. et.al.2007)

Nosocomial infections are the most common complications affecting hospitalized patients. About 25% of nosocomial infections apply to patients in the ICU, and almost 70% of these infections are caused by microorganisms that are enemseria (Austin DJ et.al.1999)(Sinha M, Srinivasa H.2007). However, other study showed that nurses' opinion was somewhat different; resistant to one or more antibiotics (Eggimann P, Pittet D.2001) Accordingly, it was not surprising that about half of the pharmacists in the study population were aware that prolonged hospital stay is a major contributor to greater bacterial resistance. Moreover, about half of the responding pharmacist thought that the other factors that are likely to contribute to bacterial resistance include the use of antibiotics without prescription and inappropriate antibiotic use, while other studies mentioned that the nurses pointed to the use of antibiotics without prescription and prescribing antibiotics when no blood culture is performed. In the pharmacists' responses, the focus was on the handling of antibiotics. A high percentage of pharmacists shared an opinion that such factors as the use of antibiotics without prescription, inappropriate antibiotic use, together with improper prescription of antibiotics are the leading causal factors of the emergence of bacterial resistance. The discrepancies in the level of awareness of bacterial resistance that were noted between pharmacists and other medical staff can be explained taking into account the medical background of each profession and the field of clinical practice. While the physicians tend to focus more on the diseases and pathogenesis, the pharmacists pay more attention to medications and an improper handling of pharmaceuticals. Moreover, the physicians and nurses are in a closer contact with patients during hospitalization than are the pharmacists. These differences in practice may also add to the different views expressed by representatives of particular medical professions.

It is alarming that neither the high rate of patients transferred between different hospital units, nor the patients' non-compliance with infection control guidelines, have been considered the factors leading to bacterial resistance. Actually, many studies have shown that the latter two are the major contributors to the emergence of bacterial resistance (Wybo I.and et.al.2007)(Thomas JK.and et.al.1999)(Pechere JC.2001).

When the risk factors for bacterial resistance are identified, effective measures should be undertaken to reduce the risk of future resistant infections. The strategies for limiting bacterial resistance are consistently discussed in literature. The adoption of certain guidelines, practice parameters, clinical pathways, or protocols, is associated with more appropriate antibiotic use, improved patient outcomes, fewer adverse events and errors, and more importantly, minimized resistance emergence (Okeke et al.2005). Since nosocomial infections highly contribute to poor outcomes and increased rates of bacterial resistance, hospitals should play a major role in limiting bacterial resistance. Better infection control strategies in hospitals and regular efficiency checks on these strategies must be put to practice. Such strategies should include reducing unnecessary hospital stay, avoiding or shortening the use of invasive devices, adhering to hand hygiene guidelines, and applying antimicrobial cycling and combination strategies (Okeke et al.2005)(Fish DN, Ohlinger MJ.2003)(burke JP.2001) The participants of our study showed a significant awareness of the above approaches. The pharmacists concentrated on the necessity to apply appropriate infection control practices ,as compare with other study in which the medical staff , the nurses focused on hygiene practices and the pharmacists were concerned with a better adherence to the infection control guidelines.

To sum up, the study has revealed a number of discrepancies in the level of awareness among the pharmacists, with respect to the frequently encountered resistant bacterial strains, the factors contributing to antimicrobial resistance and the strategies to limit this adverse phenomenon. Therefore, continuous medical education programs would be desirable to keep the health care professionals updated and diminish the future risk of excessive bacterial resistance. A 2014 WHO report, “The role of pharmacist in encouraging prudent use of antibiotics and averting antimicrobial resistance: a review of policy and experience in Europe”, (Crawford , 2007) presents a number of issues that policymakers may wish to consider with a view to strengthening their efforts to tackle AMR, such as enhancing the prudent use of antibiotics. The report was developed by the Health Technology and Pharmaceutical Programs in collaboration with WHO-EURO regional office, the Pharmaceutical Group of the European Union (PGEU), Europharm Forum, and the WHO

Collaborating Centre for Drug Development and Pharmacy Practice at Pharmakon (Denmark). Pharmacists have decisive role in combating antibiotic resistance, says new WHO European survey" (Cunha ,2005) highlighted pharmacists' roles in AMR prevention and control, following a survey carried out by the WHO-EURO regional office.

The PGEU in its statement "Community pharmacists' contribution to the control of antibiotic resistance" (Ayliffe ,1997) focused on the pharmacist's role in correcting the misconception that antibiotics are needed to treat colds and other minor ailments ,Community pharmacists are often the first point of contact for the public and they have a pivotal role in advising patients on minor ailments and referring them to their physician when required. They are often the entry gate to the health system on account of their easy accessibility.

That accessibility has been evaluated in Australia, where a study indicates that, between July 2011 and July 2012, 94% of Australians aged 18 years and over reported visiting a community pharmacy. This proportion increases to 99% for Australians aged 65 years and over. (Plata, et al ,2009) This situation gives pharmacists the unique opportunity to offer an effective medication therapy management and counseling on consumption of medicines and also engage patients in their appropriate, efficacious, safe and responsible use, as well as consulting and collaborating with physicians to ensure optimal and responsible use of antibiotics. (Elkin , Geddes , 2003)

Due to their special position in the community, pharmacists can educate and lead the general public in their (antimicrobial) medication-related needs. Roles played by community pharmacists include health promotion and infection minimization or control, triage and optimal treatment management.

Conclusions

1- Pharmacists are the most accessible health care professionals, and are fully competent in all aspects of medicines. They possess scientific knowledge for the entire medicines-use process, including procurement, preparation, storage, security, distribution, dispensing, administration and safe disposal.

2- Pharmacists are on the front line of community health services, and are the entry point for patients to health care and the health system. This position gives them various opportunities. Pharmacists serve as communicators and educators on healthy behaviors and infection prevention. They increase the coverage of immunization in hard-to-reach groups, and they are in good position to explain the importance of using antimicrobials only when needed.

3- The pharmacy is a place where pharmacists evaluate the needs of patients and provide a sort of triage. In this process pharmacists assess whether they can successfully treat the patient or whether the patient needs to be referred to another health care professional. Depending on the results of the assessment, there are three possible outcomes: the patient can be treated by the pharmacist without antibiotics, the patient can be treated by the pharmacist with antimicrobial treatments where this is legally allowed to happen, or the patient can be referred to another health care professional, usually a physician or a specialist.

4- Where pharmacists are legally allowed to prescribe antibiotics, fast and reliable diagnostic tests can support them in the proper diagnosis of common infections such as chlamydia or Lyme disease.

5- Pharmacists provide effective medication management for both short- and long-term treatments. They support adherence, minimize interactions and ensure quality of medicines. In hospitals, pharmacists lead stewardship programs and are competent in hygiene and sterilization. Pharmacists collect unused medicines, reducing the presence of antimicrobials in the environment.

6- Pharmacists are fully committed to supporting the development of programs to combat AMR, through promotion, prevention and control of antimicrobial treatments, and providing access to high quality treatments in the community and at all levels or care. Pharmacists encourage the commitment of all health care professionals to fight the AMR threat via programs developed in collaboration with stakeholders.

7- All of the above can help to prevent AMR in the community and in hospitals, and increases the likelihood of successful antimicrobial policies being implemented. This document clearly articulates the important role of pharmacists in addressing this public health issue and can provide a foundation for discussion among various stakeholders.

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Comparison between each state of the questionnaires (Appendix 1)

Q21 & Q22	0.056	Not
Q21 & Q23	0.040	Sig
Q21 & Q24	0.111	Not
Q21 & Q25	0.446	Not
Q22 & Q21	0.056	Not
Q22 & Q23	0.020	Sig
Q22 & Q24	0.017	Sig
Q22 & Q25	0.206	Not
Q23 & Q21	0.040	Sig
Q23 & Q22	0.020	Sig
Q23 & Q24	0.025	Sig
Q23 & Q25	0.260	Not
Q24 & Q21	0.111	Not
Q24 & Q22	0.017	Sig
Q24 & Q23	0.025	Sig
Q24 & Q25	0.130	Not
Q25 & Q21	0.446	Not
Q25 & Q22	0.206	Not
Q25 & Q23	0.260	Not
Q25 & Q24	0.130	Not
Q31 & Q32	0.154	Not
Q31 & Q33	0.033	Sig
Q31 & Q34	0.042	Sig
Q31 & Q35	0.208	Not
Q31 & Q36	0.076	Not
Q31 & Q37	0.005	Sig
Q31 & Q38	0.092	Not
Q31 & Q39	0.661	Not
Q31 & Q310	0.737	Not
Q32 & Q31	0.154	Not
Q32 & Q33	0.048	Sig
Q32 & Q34	0.037	Sig
Q32 & Q35	0.031	Sig
Q32 & Q36	0.030	Sig
Q32 & Q37	0.106	Not
Q32 & Q38	0.009	Sig

Q32 & Q39	0.261	Not
Q32 & Q310	0.283	Not
Q33 & Q31	0.033	Sig
Q33 & Q32	0.048	Sig
Q33 & Q34	0.001	Sig
Q33 & Q35	0.083	Not
Q33 & Q36	0.011	Sig
Q33 & Q37	0.014	Sig
Q33 & Q38	0.016	Sig
Q33 & Q39	0.440	Not
Q33 & Q310	0.500	Not
Q34 & Q31	0.042	Sig
Q34 & Q32	0.037	Sig
Q34 & Q33	0.001	Sig
Q34 & Q35	0.075	Not
Q34 & Q36	0.010	Sig
Q34 & Q37	0.019	Sig
Q34 & Q38	0.010	Sig
Q34 & Q39	0.422	Not
Q34 & Q310	0.477	Not
Q35 & Q31	0.208	Not
Q35 & Q32	0.031	Sig
Q35 & Q33	0.083	Not
Q35 & Q34	0.075	Not
Q35 & Q36	0.035	Sig
Q35 & Q37	0.162	Not
Q35 & Q38	0.037	Sig
Q35 & Q39	0.157	Not
Q35 & Q310	0.207	Not
Q36 & Q31	0.076	Not
Q36 & Q32	0.030	Sig
Q36 & Q33	0.011	Sig
Q36 & Q34	0.010	Sig
Q36 & Q35	0.035	Sig
Q36 & Q37	0.049	Sig
Q36 & Q38	0.008	Sig
Q36 & Q39	0.328	Not

Q36 & Q310	0.391	Not
Q37 & Q31	0.005	Sig
Q37 & Q32	0.106	Not
Q37 & Q33	0.014	Sig
Q37 & Q34	0.019	Sig
Q37 & Q35	0.162	Not
Q37 & Q36	0.049	Sig
Q37 & Q38	0.057	Not
Q37 & Q39	0.588	Not
Q37 & Q310	0.653	Not
Q38 & Q31	0.092	Not
Q38 & Q32	0.009	Sig
Q38 & Q33	0.016	Sig
Q38 & Q34	0.010	Sig
Q38 & Q35	0.037	Sig
Q38 & Q36	0.008	Sig
Q38 & Q37	0.057	Not
Q38 & Q39	0.322	Not
Q38 & Q310	0.363	Not
Q39 & Q31	0.661	Not
Q39 & Q32	0.261	Not
Q39 & Q33	0.440	Not
Q39 & Q34	0.422	Not
Q39 & Q35	0.157	Not
Q39 & Q36	0.328	Not
Q39 & Q37	0.588	Not
Q39 & Q38	0.322	Not
Q39 & Q310	0.016	Sig
Q310 & Q31	0.737	Not
Q310 & Q32	0.283	Not
Q310 & Q33	0.500	Not
Q310 & Q34	0.477	Not
Q310 & Q35	0.207	Not
Q310 & Q36	0.391	Not
Q310 & Q37	0.653	Not
Q310 & Q38	0.363	Not
Q310 & Q39	0.016	Sig

AWARENESS OF BACTERIAL RESISTANCE

Q41 & Q42	0.003	Sig
Q41 & Q43	0.113	Not
Q41 & Q44	0.285	Not
Q41 & Q45	0.170	Not
Q41 & Q46	0.115	Not
Q41 & Q47	0.005	Sig
Q41 & Q48	0.000	Sig
Q41 & Q49	0.015	Sig
Q41 & Q410	0.115	Not
Q42 & Q41	0.003	Sig
Q42 & Q43	0.131	Not
Q42 & Q44	0.291	Not
Q42 & Q45	0.166	Not
Q42 & Q46	0.122	Not
Q42 & Q47	0.012	Sig
Q42 & Q48	0.003	Sig
Q42 & Q49	0.017	Sig
Q42 & Q410	0.117	Not
Q43 & Q41	0.113	Not
Q43 & Q42	0.131	Not
Q43 & Q44	0.065	Not
Q43 & Q45	0.047	Sig
Q43 & Q46	0.013	Sig
Q43 & Q47	0.140	Not
Q43 & Q48	0.124	Not
Q43 & Q49	0.056	Not
Q43 & Q410	0.410	Not
Q44 & Q41	0.285	Not
Q44 & Q42	0.291	Not
Q44 & Q43	0.065	Not
Q44 & Q45	0.025	Sig

Q44 & Q46	0.042	Sig
Q44 & Q47	0.341	Not
Q44 & Q48	0.302	Not
Q44 & Q49	0.177	Not
Q44 & Q410	0.691	Not
Q45 & Q41	0.170	Not
Q45 & Q42	0.166	Not
Q45 & Q43	0.047	Sig
Q45 & Q44	0.025	Sig
Q45 & Q46	0.012	Sig
Q45 & Q47	0.222	Not
Q45 & Q48	0.183	Not
Q45 & Q49	0.087	Not
Q45 & Q410	0.521	Not
Q46 & Q41	0.115	Not
Q46 & Q42	0.122	Not
Q46 & Q43	0.013	Sig
Q46 & Q44	0.042	Sig
Q46 & Q45	0.012	Sig
Q46 & Q47	0.154	Not
Q46 & Q48	0.127	Not
Q46 & Q49	0.050	Sig
Q46 & Q410	0.433	Not
Q47 & Q41	0.005	Sig
Q47 & Q42	0.012	Sig
Q47 & Q43	0.140	Not
Q47 & Q44	0.341	Not
Q47 & Q45	0.222	Not
Q47 & Q46	0.154	Not
Q47 & Q48	0.003	Sig
Q47 & Q49	0.033	Sig
Q47 & Q410	0.082	Not

Q48 & Q41	0.000	Sig
Q48 & Q42	0.003	Sig
Q48 & Q43	0.124	Not
Q48 & Q44	0.302	Not
Q48 & Q45	0.183	Not
Q48 & Q46	0.127	Not
Q48 & Q47	0.003	Sig
Q48 & Q49	0.019	Sig
Q48 & Q410	0.104	Not
Q49 & Q41	0.015	Sig
Q49 & Q42	0.017	Sig
Q49 & Q43	0.056	Not
Q49 & Q44	0.177	Not
Q49 & Q45	0.087	Not
Q49 & Q46	0.050	Sig
Q49 & Q47	0.033	Sig
Q49 & Q48	0.019	Sig
Q49 & Q410	0.207	Not
Q410 & Q41	0.115	Not
Q410 & Q42	0.117	Not
Q410 & Q43	0.410	Not
Q410 & Q44	0.691	Not
Q410 & Q45	0.521	Not
Q410 & Q46	0.433	Not
Q410 & Q47	0.082	Not
Q410 & Q48	0.104	Not
Q410 & Q49	0.207	Not
Q51 & Q52	0.826	Not