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Incidence of Antibiotic Resistance Bacteria in Jeddah's Ministry of Health Hospitals, Saudi Arabia

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Abstract

This study aimed to determine the emergence and spread of resistant bacteria in Jeddah Ministry of Health hospitals. Sixteen month follow-up (January 2010 to April 2011) study was carried out and clinical isolates of hospitalized patients were collected, identified and their antimicrobial resistance was determined using two automated systems, Phoenix and Vitek 2. Results revealed that 6195 isolates were identified of which 94% (5846/6195) were Gram negatives. In *Escherichia coli*, the resistance was 40% (681/1703) to ciprofloxacin, 30% (511/1703) to cefepime, 29% (494/1703) to ceftazidime, 8.5% (145/1703) to tazocin and amikacin, 40% (681/1703) to gentamicin and cefuroxime. In *Klebsiella* pneumonia, the resistance was 48% (550/1147) to ceftazidime, 49% (565/1147) to cefuroxime, 45.5% (522/1147) to cefepime, 38% (436/1147) to gentamicin, 30% (344/1147) to ciprofloxacin, 19% (218/1147) to tazocin, 7.5% (86/1147) to amikacin and 2.4% (27/1147) to imipenem/meropenem. In *Acinetobacter bumannii*, 79% (850/1076) were resistant to ciprofloxacin, 68.5% (737/1076) to tazocin, 67% (721/1076) to cefepime, 66% (710/1076) to gentamicin and imipenem/meropenem, 65% (699/1076) to ceftazidime, 68% (735/1076) to amikacin and no resistance to colistin was reported. In *Pseudomonas aeruginosa*, almost 34% (555/1632) were resistant to ceftazidime, 31% (506/1632) to ciprofloxacin, 29% (473/1632) to cefepime, 26.5% (434/1638) to gentamicin, 19% (310/1632) to imipenem/meropenem, 17% (277/1632) to amikacin, and 15.5% (253/1632) were resistant to tazocin. In Gram positive isolates, MRSA counted only for 4.6% (302/6552) and no vancomycin intermediate *Staphylococcus aureus* (VISA) were detected. In conclusion, the resistance detected in this study is considered high and antibiotic Stewardship Programs is inevitably required.

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Keywords

Resistance, Clinical Isolates, Jeddah, *Klebsiella*, Antibiotic

1. Introduction

In Kingdom of Saudi Arabia, Jeddah is the second largest city with commercial importance and with a population of 3.2 million people. It is the gateway to the holy cities of Makkah and Medina [1]. The Ministry of Health oversees Jeddah's health system and provides free medical care to Saudi citizens and legal residents. The Ministry of Health in Saudi Arabia is a major source of medical services in the country and has 12 different hospitals distributed among the city with approximately a total of 2400 beds. The infection prevention and control program in those hospitals is covered by one specialized administration that runs a scientifically based standardized program. All microbiology results and antibiotic susceptibilities are sent to the administration on a monthly basis for follow-up and analysis. Data are checked for validly and accuracy with the microbiologists in the hospitals.

Antimicrobial drugs decreased death and illness associated with infectious diseases in however there is an emergence and spread of drug-resistance isolates among bacteria [2]. Antibacterial resistant isolates caused outbreaks, and more involved in health care-associated infections: including bacteremia, pneumonia, meningitis, urinary tract infection, and wound infection and greatly limited the therapeutic options for infected patients [3]. Moreover, the developed resistance for a major class of antimicrobial drugs appeared as short as 1 year to >10 years [4]. What's more, there is a major increase in the emergence and spread of multidrug-resistant bacteria to newer compounds, such as cephalosporins and fluoroquinolones [5].

The more problematic drug-resistant pathogens include multidrug-resistant *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa* among the gram-negative bacteria and methicillin-resistant *Staphylococcus aureus*, penicillin-resistant *Streptococcus pneumoniae*, and vancomycin-resistant enterococci among the gram-positive bacteria [6].

Some *E. coli* isolates caused urinary tract infection, meningitis, peritonitis intestinal and extra-intestinal infections and their resistance for the longest used antimicrobial agents was consistently the highest [7]. During a 12-year period (1971-1982), the susceptibility of *E. coli*, isolated from hospitals, showed no major change in resistance to all tested antimicrobial drugs [7]. In contrast, *E. coli* collected during 1997-2007 from urine specimens showed increasing resistance to ciprofloxacin, trimethoprim/sulfamethoxazole, and amoxicillin/clavulanic acid [8]. In a 30-year (1979-2009) follow-up study in Sweden, *E. coli* showed an increasing resistance towards ampicillin, sulfonamide, trimethoprim, and gentamicin [9] and this yet was a great concern.

In intensive care units, *Klebsiella* spp. is among the most common isolated pathogens and the emergence of *K. pneumoniae* resistance to antibiotics is well documented [10]. The study of Sanchez *et al*. [11] showed that *K. pneumoniae* antimicrobial drug resistance increased for every antimicrobial class studied except tetracyclines and cross-resistance among imipenem-resistant *K. pneumoniae* was high for ciprofloxacin but lower for amikacin and tetracycline.

Pseudomonas aeruginosa, associated with nosocomial infections, rapidly developed resistance to multiple classes of antibiotics and the import of resistance mechanisms on mobile genetic elements was always a concern [12]. Multi-drug-resistant *P. aeruginosa* was intermediate or resistant to at least three drug classes: β-lactams, carbapenems, aminoglycosides, and fluoroquinolones and the reported rates varied from 0.6% - 32% based on geographic location and the type of surveillance study [13]. Increasing emergence and spread of resistant *Acinetobacter* strains to the first and second generation cephalosporins started since 1975 but during 1980s to 1990s, the worldwide spread of imipenem resistant strains was recorded that could combat many severe *Acinetobacter* infections. Furthermore, carbapenem resistance in the strains of *A. baumannii* decreased the therapeutic options and made the life of treating physicians and patients really miserable [14]. The aim of the study was to detect the incidence of resistance in clinical bacterial isolates that was identified in 12 hospitals at Jeddah.

2. Material & Methods

Bacterial Identification and Sensitivity

The study was conducted for 16 months (January 2010 to April 2011) in 12 Ministry of Health hospitals in Jed-

dah, Saudi Arabia. During that period, 6195 non-repetitive clinical isolates from various specimens of hospitalized patients were collected and tested against the routinely used antibiotics. Two main automated systems are available and used in Jeddah hospitals laboratories; Phoenix (Becton Dickinson Diagnostic Systems, Sparks, MD, USA) and Vitek 2 (bioMérieux, Marcy l'Étoile, France). Susceptibilities of the Gram negative isolates were tested to the following antibacterial agents: Ceftazidime, Ciprofloxacin, Cefepime, Amikacin, Tazocin, Gentamicin, Cefuroxime and Imipenem. Colistin was tested only when an isolate showed a complete pattern of resistance to all tested antibiotics. All bacterial isolates were tested using standard bacteriological procedures and according to the procedures recommended by the manufacturers. No attempt was made to compare between the results of the two methods in this study.

3. Results

Sixteen month follow-up (January 2010 to April 2011) of the clinical isolates, obtained from hospitalized patients, in the 12 Ministry of Health hospitals was carried out. The counts and resistance of some of the Gram positive and negative bacterial isolates were identified using in-house diagnostic microbiology methods. **Figure 1** revealed that 6195 isolates were identified of which 94% (5846/6195) were Gram negatives and 6% (637/6195) were Gram positive. Furthermore, *E. coli* was the most isolated organism and counted for 27% (1703/6195) of all identified isolates followed by *P. aerignosa* 26% (1632/6195), *K. pneumoniae* 18% (1147/6195), *Acinetobacter bumannii* 17% (1076/6195) and *Enterobacter cloacae* 4.6% (288/6195). MRSA counted for almost 5% (349/6195) and *Streptococcus pneumoniae* for 0.7% (47/6195). The rate of resistance in Gram negative isolates is shown in **Figures 2-5**.

In *Escherichia coli*; 40% (681/1703) were resistance to ciprofloxacin, gentamicin or cefuroxime, 30% (511/1703) were resistant to cefepime, 29% (494/1703) to ceftazidime, 8.5% (145/1703) to tazocin and amikacin, 40% (681/1703) to (**Figure 2**). In *Klebsiella pneumonia* isolates, 48% (550/1147) were resistant to ceftazidime, 49% (565/1147) to cefuroxime, 45.5% (522/1147) to cefepime, 38% (436/1147) to gentamicin, 30% (344/1147) to ciprofloxacin, 19% (218/1147) to tazocin, 7.5% (86/1147) to amikacin and 2.4% (27/1147) to imipenem/meropenem (**Figure 3**). In *A. bumannii*, 79% (850/1076) were resistant to ciprofloxacin, 68.5% (737/1076) to tazocin, 67% (721/1076) to cefepime, 66% (710/1076) to gentamicin and imipenem/meropenem, 65% (699/1076) to ceftazidime, 68% (735/1076) to amikacin and no resistance to colistin was reported (**Figure 4**). In *Pseudomonas aeruginosa*, almost 34% (555/1632) were resistant to ceftazidime, 31% (506/1632) to ciprofloxacin, 29% (473/1632) to cefepime, 26.5% (434/1638) to gentamicin, 19% (310/1632) to imipenem/meropenem, 17% (277/1632) to amikacin, and 15.5% (253/1632) were resistant to tazocin (**Figure 5**).

In Gram positive isolates; out of 357 *Staphylococcus aureus* isolates collected, 302 (89%) were MRSA which counted only for 4.6% (302/6552) of the total collected isolates. No vancomycin intermediate *Staphylococcus*

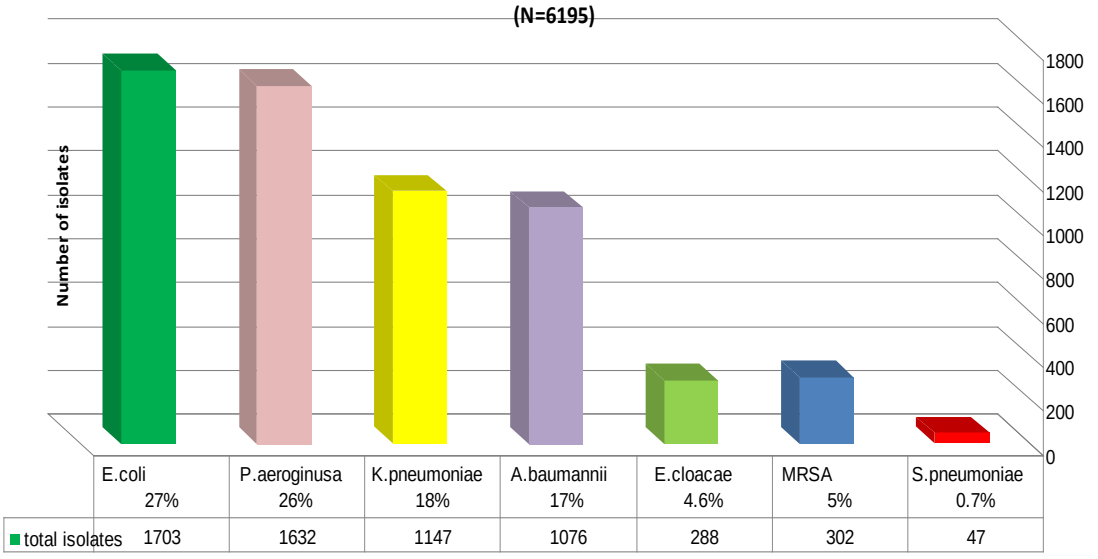

Figure 1. The different pathogenic bacterial isolates and their rates.

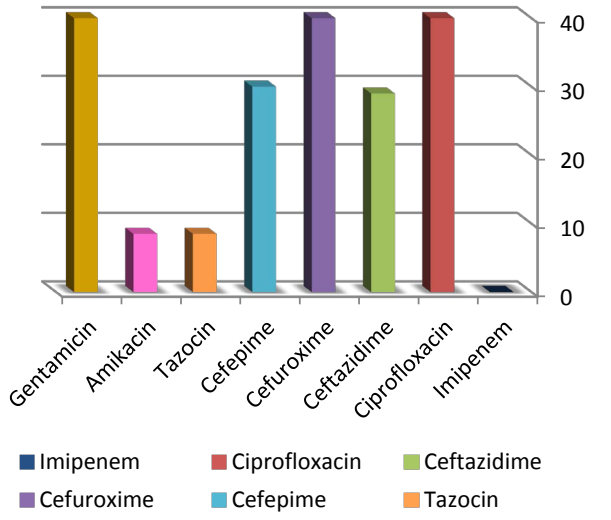

Figure 2. The overall resistance rate of *E. coli* isolates (N = 1703) to different used antibiotics.

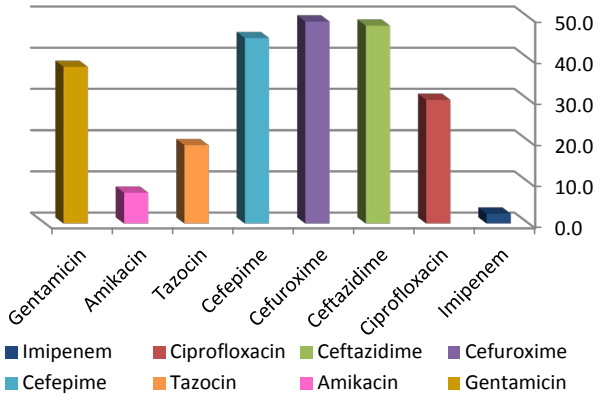

Figure 3. The overall resistance rate of *K. pnermoniae* isolates (N = 1147) to different used antibiotics.

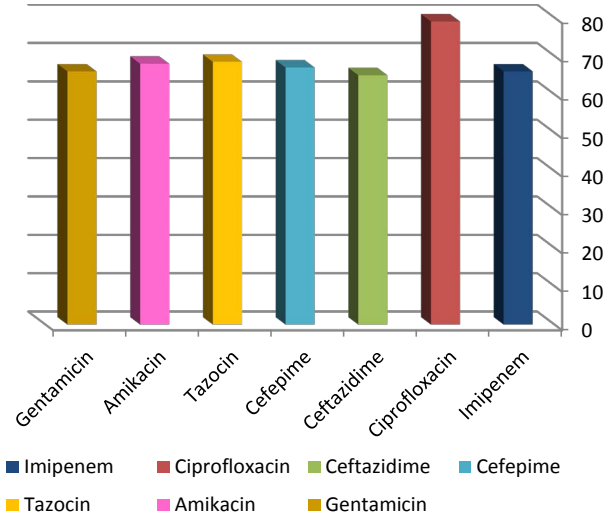

Figure 4. The overall resistance rate in *A. bumannii* isolates (N = 1076) to different used antibiotics.

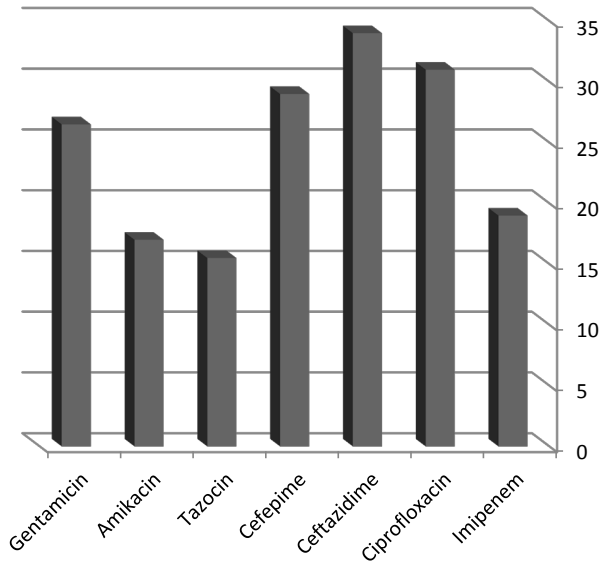

Figure 5. The overall resistance rate in *P. aeruginosa* isolates (N = 1632) to different used antibiotics.

aureus (VISA) were detected. Furthermore, only 10% (5/47) *Streptococcus pneumonia* isolates were resistant to penicillin (data not shown).

4. Discussion

Bacterial pathogens have a great ability to adapt and overcome the challenges of antibiotics in their environment that threaten to move us into the "post-antibiotic era" of infectious diseases. The therapy for resistant bacterial infections becomes more problematic than ever and the infection prevention is now very essential [15] [16]. Our study has some limitations where identification of the multi-drug resistance isolates is performed with two different automated systems and this may have given slight variations of the antibiotics' break points. Hence, standardization of lab identification methodologies in all hospital labs might be desirable.

Our study revealed *E. coli* is the dominating organism (27%) in comparison to other Gram negatives bacteria. In addition, *P. aeruginosa* was found to be the second isolated organism (26%) which might highlight the heavy involvement of hospital environment. Lower percentages 18% and 17% were recorded in *K. pneumoniae* and *A. baumonnii*, respectively. In a study that was conducted by Wagenlehner *et al*. [17], *E. coli* counted for 50% of the yielded isolates, *Proteus* spp. 15%, *Klebsiella* spp. 15% and *P. aeruginosa* 5%. The resistance rates reported in this study was disturbing to ciprofloxacin, gentamicin or cefuroxime (40%) in *E. coli*, to cefuroxime (49%) and ceftazidime (48%) in *K. pneumonia*. Similarly, Livermore *et al.* [18] reported the changes in susceptibility pattern of *E. coli* and during 2011 in Central Greece, a significant increase in *E. coli* ciprofloxacin resistance (21%) has occurred [19]. The emergence of extended resistant *Acinetobacter* spp. was rapidly spreading to even newer antimicrobials and they acquired resistance faster than other Gram-negative organisms due to their ease of survival in the hospital environment, their immense potential to cause nosocomial outbreaks and their biofilm forming ability which played a crucial role in their *in-vitro* and *in-vivo* survival [20]. This study showed that ≥66% of *A. bumannii* isolates were resistant to almost all tested antibiotics and this clearly indicated how problematic to have patients infected with this organism and the minimal chances available to find proper treatment.

Increasing resistance of *P. aeruginosa* to the various antipseudomonal agents has been reported worldwide which cause a serious problem in infection management. Although up to 34% of *P. aeruginosa* in our study isolates were resistant to ceftazidime and 31% to Ciprofloxacin, other alternative antibiotics are available. This high resistance clearly indicates the overuse of the latter antibiotics and insists the demand of a strictly respected comprehensive antibiotic stewardship program in our hospitals. In United States, a dramatic antimicrobial resistance increase to ciprofloxacin (from 15% to 32%) and ceftazidime (from 15% to 19%) over the ten-year period was recorded [21]. In Kuala Lumpur, Malaysia, approximately 10% of clinical isolates of *P. aeruginosa* were resistant to imipenem, while 11% showed resistance to ciprofloxacin, piperacillin and ceftazidime [22] [23].

Despite the increasing resistance to ceftazidime, it was still in use against *P. aeruginosa* infections as the resistance did not exceed 35% in our study.

Staphylococcus aureus cause health care-associated infections for both hospitalized patients with healthy or decreased host defenses. In the 1980s, methicillin-resistant *S. aureus* (MRSA) emerged as a major clinical and epidemiologic problem in hospitals and spreaded out of the hospitals into communities. In the present study, MRSA counted only for 4.6% of the total collected isolates and 89% of *S. aureus* isolates which probably indicated the need for better understanding to infection control measures in the hospitals. Prevalence of MRSA in hospitals increased from 2.1% in 1975 to 35% in 1991 [24] and it was 46% in Western Pacific region, 5.7% in Canada, varied from less than 2% in the Netherlands to 54.4% in Portugal, from 23.6% in Australia to more than 70% in Japan and Hong Kong [25] [26] and 30% - 60% in Thailand [27]. For serious MRSA infections, vancomycin is the treatment of choice and MRSA strains with reduced susceptibility to vancomycin have been reported [28] [29] but in this study no vancomycin resistant isolates were found. Only 10% of *S. pneumonia* isolates were resistant to penicillin which might indicate that the resistance to this bacteria in particular was not very high. However, this rate might increase if more awareness were not really considered at this stage. Hofmann *et al*. [30] reported that 25% of the isolates were resistant to penicillin. This may indicates that more resistant *S. pneumonia* isolates are on the way.

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