Bahrain Medical Bulletin, Vol. 34, No.4, December 2012

Trends of Empiric Antibiotic Usage in an Accident and Emergency Department in a Secondary Care Hospital

Jameela Al Salman, MD* Aysha Husain, MD** Muneer Mahdi, MD**

Background: Several strategies to optimize the use of antibiotics have been developed. Most of these interventions can be classified as educational or restrictive. Restrictive measures are considered to be more effective, but the enforcement of these measures may be difficult and may lead to conflicts with prescribers. Any intervention should be aimed at targets with the highest impact on antibiotic prescribing[1].

Objective: To evaluate the current practices of prescribing antibiotics at the time of admission and to assess the adequacy of empiric antibiotic use and to identify risk factors for inadequate treatment and targets for intervention.

Design: A prospective observational study.

Setting: Salmaniya Medical Complex.

Method: From November 2007 to March 2008, patients admitted in the medical department through the emergency and who received antibiotic therapy within 24 hours were included. Antibiotic therapy was considered adequate if the spectrum of coverage, dose, application mode and duration of therapy were appropriate according to local recommendations or published international guidelines.

Result: Two hundred admitted patients were evaluated. One hundred nineteen patients' records were traced and evaluated after patients were discharged. Twenty (16.8%) patients received antibiotics within 4 hours; 99 (83.2%) had their first dose of antibiotics within 24 hours of admissions. Empirical antibiotic therapy was inadequate in 14 (11.8%) patients. Initial therapy was adjusted in 61 (51.3%) patients.

Conclusion: We found a high rate of inappropriate empiric antibiotic use in our institution, which is similar to other studies. A well-structured and organized antimicrobial team has to be established to implement antimicrobial management program in the hospital. That will ultimately improve the rate of inadequate antibiotic use.

Bahrain Med Bull 2012; 34(4):

Because of the increasing concern and awareness of antibiotic resistance worldwide and their frequent inappropriate use, they became the target of restriction and control[2]. In our hospital,

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* Chairman
** Senior Resident
Medical Department
Salmaniya Medical Complex
Kingdom of Bahrain
Email: jalsalman@hotmail.com

an antibiotic policy was established since 2008. It was circulated and was monitored over a period of three years. We found that the rate of compliance of physicians was very low.

Antibiotic resistance of bacteria is an increasing, worldwide problem[3]. One of the most important attributing factors to this serious problem is the increasing incidence of inappropriate use of antibiotics. It was found in several studies that a large number of antibiotics are prescribed without a clear indication[3,4].

In order to reduce the rate of antibiotic misuse, a well-organized and effective antimicrobial program has to be implemented in all health care facilities. The purpose of this program is to evaluate and audit the daily use of antibiotics, apply an educational program and a restrictive policy[5,6].

The rate of inappropriate antibiotic use reached up to 43% in some studies[7]. These data and their relationship to the rate of increased multi-drug resistant organisms have led to the heightened importance of an infectious diseases expert in each health care facility in order to minimize the magnitude of the problem.

Recent studies examining the overuse of antimicrobials in hospitals have focused on specific patient populations or specific indications[8]. Multi-drug resistant organisms will overgrow and ultimately cause infection in a susceptible individual[9].

One of the main objectives of an antimicrobial program is to collect the data of the pattern of antibiotic prescription and trends; based on that, the areas of misuse will be identified[7].

The aim of this study is to evaluate the current practices of prescribing empiric antibiotics at the time of admission to the hospital and to assess their appropriateness.

METHOD

Patients admitted during the period from November 2007 to March 2008 to the medical department and needed empirical antibiotics were included.

Personal characteristics, admission diagnoses, empirical antibiotic, duration of therapy, specimens culture and sensitivity, systemic inflammatory response syndrome (SIRS) were prospectively recorded on a case report form. After discharge, all prospectively collected data were verified and completed by chart review. Each case report and chart was reviewed by two authors, who assessed the adequacy of empirical antibiotic therapy.

Empirical antibiotic is defined as the initial regimen used within the first 24 hours of admission. Antibiotic therapy was defined as inadequate if it does not follow the local written recommendations or published guidelines (The Sanford Guide to Antimicrobial Therapy, Practice Guidelines of the Infectious Diseases Society of America), or one or more of the following points were not met: spectrum of coverage, dosage, application mode of antibiotics, the duration of therapy and bacterial sensitivity.

Data were collected on special data sheet. Data were entered into Microsoft Excel 2007 worksheets for further analysis.

RESULT

Two hundred patients were targeted, but only 119 completed the process. The remaining 81 patientsô records could not be traced. Patients who completed the process were divided into six groups: respiratory, renal, sepsis, sickle cell disease (SCD), gastrointestinal and miscellaneous group (which included: neutropenic patients, fever of unknown origin, cellulitis, etc).

Three hundred nineteen bacteriological samples were taken from 119 patients. The most commonly performed investigations were blood culture 116 (36.4%), urine culture 104 (32.6%) and sputum culture or broncho-alveolar lavage 54 (17%). Forty-one bacteriological samples were positive.

The most common bacteria from all the positive cultures were *Escherichia coli* (14 patients, 34%), *Pseudomonas aeruginosa* (6 patients, 14.6%), *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Staphylococcus epidermis* had the same percentage (4 patients, 9.7%).

The most common antibiotic used empirically was ceftriaxone (Rocephin), 60 (50.4%). About 50% of patients admitted were commenced on intravenous ceftriaxone. The second antibiotic used was erythromycin oral, 23 (19.3%). Piperacillin/tazobactam (Tazocin) ranked third in term of empirical usage, 21 (17.6%). The mean of antibiotic use was 6.4 days after admission. The empirical therapy was adjusted in 61 (51.3%). Sepsis group, 7 patients out of 9 (77.8%), was the highest to use antibiotics. The lowest was the miscellaneous group, 6 patients out of 16 (37.5%), see figure 1.

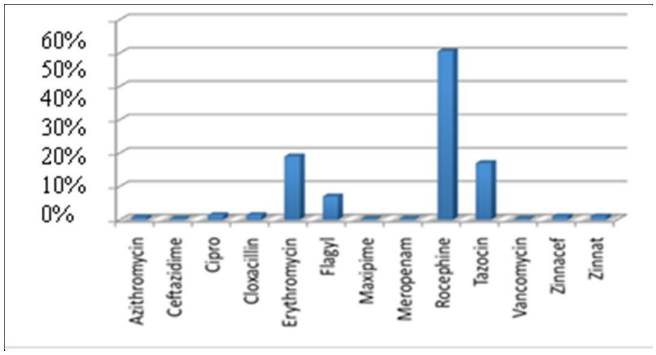

Figure 1: Frequency of Antibiotics Prescription

1. The Respiratory System Group (n=38)

Thirty-eight patients admitted under the respiratory system, the most common diagnosis is pneumonia; the most common presentation was cough and shortness of breath followed by fever, see table 1.

Table 1: Frequency of Antibiotics Usage among Respiratory Group (n=38)

Antibiotics	Number & Percentage
Rocephine	28 (73.7%)
Erythromycin	27 (71%)
Tazocin	8 (21%)
Cipro	1 (2.6%)
Zinacef	8 (21%)

The majority was treated as a community acquired pneumonia and was started on a third generation antibiotics and macrolides. Six (15.8%) patients received the antibiotics within four hours of reaching the accident and emergency department and 32 (84%) were given the antibiotics within the first 24 hours.

Blood culture was requested for 37 (97.4%) patients. The blood culture was positive in 2 (5.3%) patients who were positive for *Staphylococcus epidermidis*. Urine culture was requested for 34 (89.5%) patients but was done for 29 (76.3%). The result was contaminated in 6 (15.8%) and positive in 2 (5.3%), the organisms were *Escherichia Coli* and *Candida.*

The sputum culture was requested for 35 (92.1%) patients and was done for 25 (65.8%). The sputum culture was positive in 20 (52.6%). Three (7.9%) were positive for tuberculosis. The remaining cultures were positive for *Klebsiella/klebsiella ESBL, Yeast, Staphylococcus Aureus, Pseudomonas, E.Coli/E.Coli ESBL.*

Other cultures requested were as follow: throat, stool, wound and pleural fluid; the majority was pleural fluid culture, 10 (26.3%); the yield of pleural fluid culture was negative.

The major comorbidities we included in our study are the following: immunosuppression, organ failure, ischemic heart disease (IHD), diabetes mellitus (DM) and others. The others include the following: hemoglobinopathies other than sickle cell disease, epilepsy, hypertension, cardiomyopathies, asthma and COPD.

The most common comorbidities found in patients admitted under the respiratory service were shown in figure 2. Most of these patients have diabetes mellitus. Five deaths were recorded in this group, 3 patients required ICU stay and 3 patients required intercostal drainage insertion.

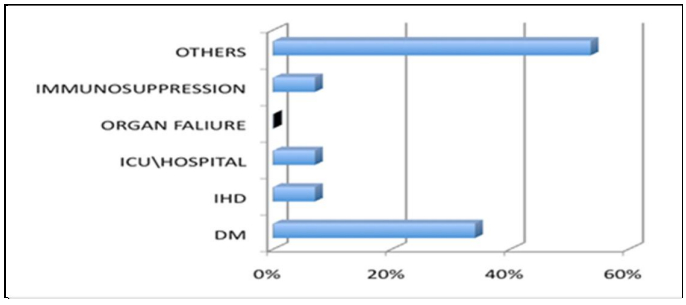

Figure 2: Frequency of Comorbidities Recorded in Respiratory Group

2. Renal Group (n=14)

Fourteen patients were admitted in this group, commonly presented with fever and fatigue. The use of antibiotics in this group is illustrated in table 2. One (7%) patient received antibiotics within 4 hours and the remaining within the 24 hours.

Table 2: Frequency of Antibiotics Usage in Renal Group (n=14)

Antibiotics	Number & Percentage*
Rocephin 2 gm od	12 (85.7%)
Rocephin 1 gm od	1 (7%)
Tazocin 4.5 gm q8	1 (7%)

* Some of the patients used more than one antibiotic

Blood culture was requested for all patients; it was positive in 4 (28.6%). Positive blood cultures showed *E.Coli, E.Coli ESBL and Klebsiella ESBL*. Urine culture was requested for all patients. The cultures were contaminated in 2 (14.3%). The cultures were positive in 4 (28.6%) specimen. Positive culture showed *E.Coli + E.Coli ESBL + Enterococci*. Sputum culture was requested for 2 (14.3%) and none was done. Stool culture was requested for 3 (21.4%) patients and was done for 2, see figure 3 for comorbidities. Diabetes ranked first in comorbidities. Two patients died in this group, one required dialysis and one had drug eruption, which necessitated change of antibiotic.

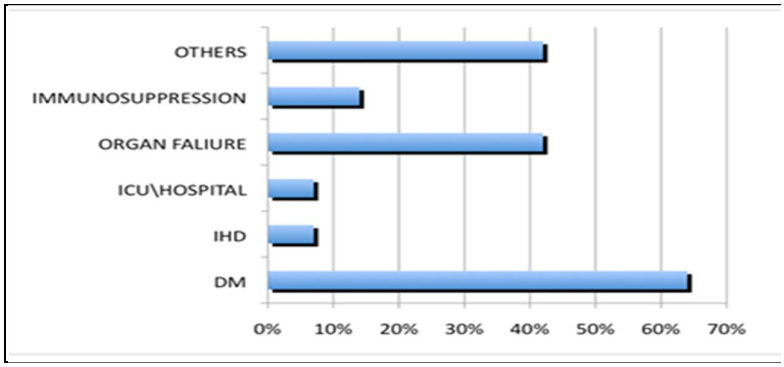

Figure 3: Frequency of Comorbidities Recorded in Renal Group

3. Sepsis Group (n=9)

Nine patients were admitted under sepsis group. The most common presentation was fever followed by reduce activity, see table 3.

Table 3: Frequency of Antibiotic Use in Sepsis Group (n=9)

Antibiotics	Number & Percentage*
Rocephine	1 (11%)
Tazocin	8 (88.8%)
Cloxacillin	1 (11%)
Azithromycin	1 (11%)

* Some of the patients used more than one antibiotic

The antibiotics were given to 2 (22.2%) patients within 4 hours and to 7 (77.8%) within the first 24 hours. Blood culture was requested for all patients, positive only in one (11%). The positive blood culture was for *staphylococcus aureus (MRSA).* Urine culture was requested for all patients, positive only in 2 (22.2%), *E.Coli ESBL* was the culprit. Sputum culture was requested for 4 (44%) patients and was done for one (11%). All of these cultures were negative. Other cultures such as throat, stool and wound were requested for 5 (55.6%) and was done for 4 (44.4%) patients. The comorbidities in this group are shown in figure 4. Diabetes mellitus was the most common comorbidity found, two patients died in this group, the cause was not determined.

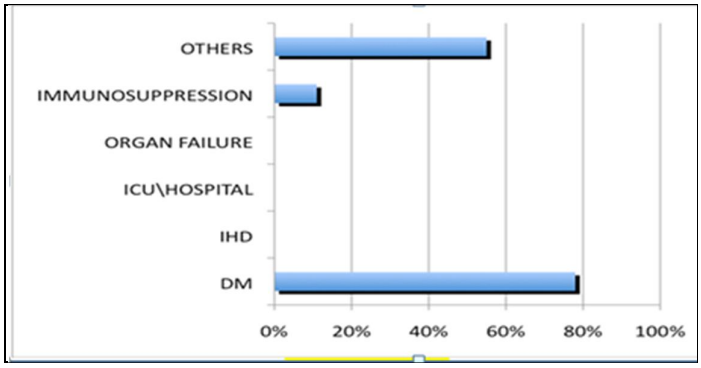

Figure 4: Frequency of Comorbidities among Sepsis Group

4. Sickle Cell Disease (SCD) Group (n=21)

Twenty-one patients were admitted in this group. The most common presentation was fever followed by vaso-occlusive crisis, pain in various regions, see table 4 for antibiotic use in this group. The antibiotics were given to 3 (14.3%) within 4 hours and to 18 (85.7%) patients within the first 24 hours.

Table 4: Frequency of Antibiotics Usage in SCD Group (n=21)

Antibiotics	Number & Percentage*
Rocephine	14 (66.7%)
Tazocin	3 (14.3%)
Cipro	1 (4.8%)
Zinacef	2 (9.5%)
Flagyl	2 (9.5%)

* Some of the patients used more than one antibiotic

Blood culture was requested for all patients; positive in one (4.8%). Positive blood cultures revealed *E.Coli*. Urine culture was requested for all patients but was done only for 12 (57%). Contamination was seen in one (4.8%) specimen, positive in one (4.8%), the microorganism was *Enterococci*. Sputum culture was requested for 6 (28.6%) patients and was done for 2 (9.5%), the positive yield was zero.

Throat and stool cultures were requested for 4 (19%) and was done for one (4.8%), positive yield was zero. No comorbidities were found in this group except for one patient who was diabetic. There was no death in this group and all of them were discharged in good condition.

5. Gastroenterology Group (n=21)

Twenty-one patients were admitted, presented with diarrhea and abdominal pain; see table 5, antibiotic use in this group. The antibiotics were given to 4 (19%) within four hours and to 17 (81%) within the first 24 hours.

Table 5: Antibiotics Use in Gastroenterology Group (n=21)

Antibiotics	Number & Percentage*
Rocephin	19 (90.5%)
Cipro 500mg bd	1 (4.8%)
Flagyl 500mg q8	7 (33.3%)
Zinnat 250mg bd	1 (4.8%)

* Some of the patients used more than one antibiotic

Blood culture was requested for all patients and was done for 20 (95.2%). The blood culture was positive in one (4.8%); most likely it was contaminated since the organism recovered is *Staph Epidermidis*. Urine culture was requested for 15 (71.4%) patients but was done for 11 (52.4%). The result was contaminated in 4 (19%) and was positive in 2 (9.5%), *E.Coli, ESBL E.Coli* and *Pseudomonas* were recovered.

Stool culture was requested for 13 (61.9%) patients and was done for 8 (38%). The positive yield was around one (4.8%), due to Shigella. Ascitic fluid culture was requested for one (4.8%), but the yield was negative.

The most common microorganism for positive urine culture was *E.Coli*, see figure 5 of comorbidities.

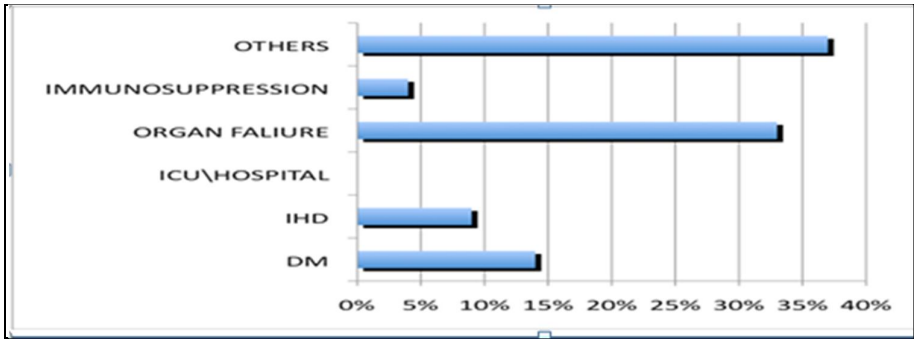

Figure 5: Frequency of Comorbidities among Gastroenterology Group

6. The Miscellaneous Group (n=16)

Sixteen patients were admitted with fever. The miscellaneous group included patients with neutropenic fever, cellulitis and fever for investigations, see table 6 for antibiotics use in the miscellaneous group.

Table 6: Number of Patients Given Antibiotics in Miscellaneous Group (n=16)

Antibiotics	Number & Percentage*
Rocephin	13 (81.3%)
Tazocin	1 (6.3%)
Vancomycin	1 (6.3%)
Erythromycin	1 (6.3%)
Cloxacillin	1 (6.3%)
Zinnat	1 (6.3%)

* Some of the patients used more than one antibiotic

Two (12.5%) received antibiotics within four hours and in 14 (87.5%) within the first 24 hours.

Blood culture was requested for 14 (87.5%) patients, positive in one (6.3%), *Staph Aureus* was recovered. The urine culture was requested for all patients but was done for 11 (68.8%), positive in 2 (12.5%), the microorganisms recovered were *Pseudomonas* and *Candida*. Sputum culture was requested for 5 (31.3%) patients and was done for 2 (12.5%). The positive yield was zero. The other cultures requested were throat, stool, wound and cerebrospinal fluid for 9 (56.3%), which had negative yield, see figure 6 for the comorbidity in this group. The most common comorbidity is diabetes mellitus. There was one death in this group, the cause was not determined.

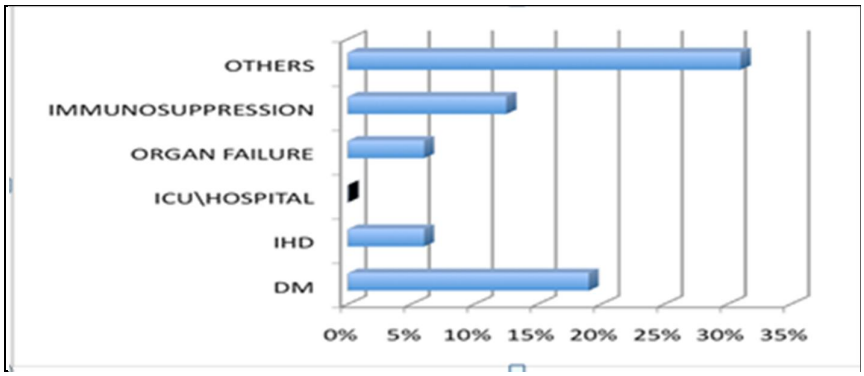

Figure 6: Frequency of Comorbidities in Miscellaneous Group

DISCUSSION

In the respiratory system group which is the largest group in the study, the third generation cephalosporin and macrolides were the most commonly used antibiotics.

According to the international guidelines for the treatment of the community acquired pneumonia, the antibiotic should cover the most common bacteria. The most common are Streptococcus pneumonia and Haemophilus influenzae; the atypical are *Legionella, Chlamydia* and *Mycoplasma*[10]. The antibiotic of choice is the combination of ɓ-lactam drug and macrolide or quinolones.

In this study, all physicians were using the first combination because third or fourth generation quinolones were not available[10-14]. The use of ɓ-lactam or the combination of ɓ-

lactam and macrolide for the community acquired pneumonia still needs randomized clinical trials[14].

In this study, the third generation cephalosporin (Ceftriaxoneï Rocephin) was the most commonly used antibiotics, that has several implications. This reflects the current clinical trends of health care workers to overprescribe the third generation cephalosporin as empiric antibiotic, even though no definitive diagnosis was reached. In our study, we found that most bacteria recovered from cultures were multi-drug resistant organisms. This means that they are resistant to our first choice for empiric antibiotic which is Rocephin. The high rate of multi-drug resistant organisms may reflect the amount of abuse of the antibiotics in the community and in the hospital. Finally, it is well documented in the literature, that the third generation cephalosporins are inducers of the ɓ-lactamases enzymes which contribute to a multi-drug resistant organism.

In our study, there was an excess use of antibiotics in the gastroenteritis group despite that all the cultures were negative and which indicated viral etiology. In our study, we noticed an increased rate of excessive use of different types of cultures. This indicates a high rate of non-compliance with the local guidelines for the diagnosis of different infective syndromes.

Special consideration has to be given to fever of non-infectious etiology, especially sickle cell patients and others who could present with simple vasoocclusive crisis and fever.

The direct and indirect increased cost of the inappropriate use of antibiotics has to be addressed in any antimicrobial program. The indirect cost is related to the management of complications and side effects of the antibiotics, intravenous tubing and intravenous catheter placement.

Several international studies were conducted to determine the reasons for inappropriate prescriptions of antibiotics. Similar studies are needed in the Kingdom of Bahrain. The most common reasons are: the degree of severity of the illness, immunocompromised patients and prescription by inexperienced physicians[15,16].

Most of these reasons could be addressed and overcome by a well-structured educational program for the health care workers in order to minimize the inappropriate prescription of antibiotics and subsequently the rate of multi-drug resistant organisms[17].

Our study has several limitations. First, we included the patients that were admitted only to the medical department, where it would be better to include other clinical subspecialties such as surgery, obstetrics and gynecology, etc.

Second, our study was based on the evaluation of the medical records of the patients not on the evaluation of the patients clinically. Medical records of patients are based on how well the documentation of the medical staff is[17].

CONCLUSION

In this study, there was an excessive use of inappropriate antibiotics. The most commonly abused antibiotic is the third generation Cephalosporin. We highly recommend establishing a well-structured antimicrobial stewardship program. This program has to start by establishing local antimicrobial guidelines based on the current

local antibiogram and the local resistant data in the hospital. A major educational program for all the health workers who are involved in antibiotic prescription about the proper use of antibiotics needs to be established, develop antibiotics restriction and monitor this process closely in order to decrease the overall morbidity and mortality in our institution.

Author Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes

Potential conflicts of interest: No

Competing interest: None **Sponsorship:** None

Submission date: 7 April 2011 **Acceptance date**: 30 August 2012

Ethical approval: Secondary Care Medical Research Sub-committee, MOH.

REFERENCES

1. Mettler J, Simcock M, Sendi P, et al. Empirical Use of Antibiotics and Adjustment of Empirical Antibiotic Therapies in a University Hospital: A Prospective Observational Study. BMC Infectious Diseases 2007; 7: 11-21.
2. Gould IM. Antibiotic Policies and Control of Resistance. Curr Opin Infect Dis 2002; 15(4): 395-400.
3. Mera RM, Miller LA, Daniels JJ, et al. Increasing Prevalence of Multidrug-Resistant Streptococcus Pneumoniae in the United States over a 10-Year Period: Alexander Project. Diagn Microbiol Infect Dis 2005; 51(3): 195-200.
4. WHO. Hospitals: Recommendations for Intervention. WHO Global Strategy for Containment of Antimicrobial Resistance. Geneva, Switzerland, WHO 2001: 26-35. whqlibdoc.who.int/hq/2001/WHO_CDS_CSR_DRS_2001.2.pdf. Accessed on 3.3.2010.
5. Brown EM. Interventions to Optimise Antibiotic Prescribing in Hospitals: The UK Approach. In: Gould IM, Meer JWM, eds. Antibiotic Policies: Theory and Practice. New York: Kluwer Academic/Plenum Publishers, 2005: 159-83.
6. Ruttimann S, Keck B, Hartmeier C, et al. Long-term Antibiotic Cost Savings from a Comprehensive Intervention Program in a Medical Department of a University-Affiliated Teaching Hospital. Clin Infect Dis 2004; 38(3): 348-56.
7. Hecker TM, Aron CD, Patel PN, et al. Unnecessary Use of Antimicrobials in Hospitalized Patients: Current Patterns of Misuse with an Emphasis on the Antianaerobic Spectrum of Activity. Arch Intern Med 2003; 163(8): 972-8.
8. Lee KR, Leggiadro RJ, Burch KJ. Drug Use Evaluation of Antibiotics in a Pediatric Teaching Hospital. Infect Control Hosp Epidemiol 1994; 15(11): 710-2.
9. Goldmann DA, Weinstein RA, Wenzel RP, et al. Strategies to Prevent and Control the Emergence and Spread of Antimicrobial-Resistant Microorganisms in Hospitals: A Challenge to Hospital Leadership. JAMA 1996; 275(3): 234-40.
10. Dudas V, Hopefl A, Jacobs R, et al. Antimicrobial Selection for Hospitalized Patients with Presumed Community-Acquired Pneumonia: A Survey of Nonteaching US

Community Hospitals. Ann Pharmacother 2000; 34(4): 446-52.
11. Martinez JA, Horcajada JP, Almela M, et al. Addition of a Macrolide to a ϐ-lactam-Based Empirical Antibiotic Regimen is Associated with Lower In-hospital Mortality for Patients with Bacteremic Pneumococcal Pneumonia. Clin Infect Dis 2003; 36(4): 389-95.
12. Lin E, Stanek RJ, Mufson MA. Lack of Synergy of Erythromycin Combined with Penicillin or Cefotaxime against Streptococcus Pneumoniae in Vitro. Antimicrob Agents Chemother 2003; 47(3): 1151-3.
13. Paul M, Nielsen AD, Gafter-Gvili A, et al. The Need for Macrolides in Hospitalised Community-Acquired Pneumonia: Propensity Analysis. Eur Respir J 2007; 30(3): 525-31.
14. Schwartz B, Bell DM, Hughes JM. Preventing the Emergence of Antimicrobial Resistance: A Call for Action by Clinicians, Public Health Officials, and Patients. JAMA 1997; 278(11): 944-5.
15. Gonzales R, Bartlett JG, Besser RE, et al. Principles of Appropriate Antibiotic Use for Treatment of Acute Respiratory Tract Infections in Adults: Background, Specific Aims, and Methods. Ann Intern Med 2001; 134(17): 479-86.
16. Avorn J, Solomon DH. Cultural and Economic Factors that (Mis) Shape Antibiotic Use: The Nonpharmacologic Basis of Therapeutics. Ann Intern Med 2000; 133(2): 128-35.
17. Scheckler WE, Bennett JV. Antibiotic Usage in Seven Community Hospitals. JAMA 1970; 213(2): 264-7.