Original Paper

A STUDY ON ANTIMICROBIAL RESISTANCE: RECENT TREND IN ARMED FORCES OF BANGLADESH

Azad MAK[1], Rahman Z[2], Amin MN[3]

Abstract

Introduction: Antimicrobial resistance has increased dramatically & to be a serious threat to the treatment of infectious disease on a global basis. As a result morbidity, mortality & economic burden of infections with multiple drug resistance organisms for which there are no effective therapies. Over use of antibiotics in developed nations of paradoxically both misuses of under use in developing nations have contributed to the burden.

Objectives: The objective of the study is to identify common microorganisms and to assess their sensitivity to three selected antibiotics.

Methods: This observational study was conducted in Armed Forces Institute of Pathology (AFIP), Dhaka, Bangladesh among samples of urine, blood, pus, sputum and throat swab. All of the samples of urine (173), Blood (31), pus (63), sputum (28) and throat swab (14) were tested for culture and sensitivity at AFIP over a period from January 2012 to February 2013. Selected antibiotics were ciprofloxacin, cephradine and cefixime.

Results: Commonest organisms found in different samples were *Escherichia coli* in urine (57.8%), *Salmonella* typhi in blood (54.8%), *Staphylococcus aureus* in pus (42.9%), *klebsiella* in sputum (67.9%) and *Streptococcus pyogens* in throat swab (78.6%). In urine samples, microorganisms were found resistant to cephradine in 95% cases but sensitive to cefixime in 30.4% cases. Microorganisms in blood samples were sensitive to cefixime in 83.3% and Ciprofloxacin in 80.6% cases. Ciprofloxacin, cephradin and cefixime all three antibiotics encountered resistance in 63.5%, 82.5% and 75.8% samples of pus respectively. Among sputum samples organisms were sensitive to ciprofloxacin in 71.4% and cefixime in 64.3% cases whereas resistant to cephradin in 92.9% cases. In organisms of throat swab Cephradine Showed sensitivity in 71.4% cases but cefixime encountered resistance in 57.1% cases.

Conclusion: The study reveals an alarming picture of antimicrobial resistance pattern in Bangladesh Armed Forces.

Key-words: Antimicrobial Resistance, Armed Forces Institute of Pathology, Bangladesh Armed Forces.

Introduction

Antimicrobial resistance is a fluid and constantly evolving challenge of modern world. It has become a major obstacle to the treatment of infectious diseases worldwide. Antibiotic resistance has increased dramatically and rapidly during the 1990s, and it is widely acknowledged to be a serious threat to the treatment of infectious diseases on a global basis.

1. **Maj Gen Md Abul Kalam Azad**, MBBS, MPH, MSc, Ph.D, Director General, Bangladesh Armed Forces Medical Services; 2. **Lt Col Zaheedur Rahman**, MBBS, MPH, Medical Officer, Bangladesh Air Force; 3. **Lt Col Md Nurul Amin**, MBBS, MPH, ADGMS (Training), Directorate General Medical Services.

The morbidity, mortality and economic burden of infections with multiple drug resistant organisms, for which there are no effective therapies, pose an increasing burden for health care systems worldwide. The WHO report, entitled Overcoming Antimicrobial Resistance gives a stark warning that, at the dawn of a new millennium, humanity is faced with a crisis, where rising rates of drug resistance in many microorganisms could rob the world of its opportunity to cure many common infectious diseases. Overuse of antibiotics in developed nations and, paradoxically, both misuse and underuse in developing nations have contributed to the burden. Due to fears of resistance, many health care providers are avoiding narrow spectrum drugs in favour of broader spectrum antibiotics that have wider applications and greater impact on the natural flora. The report also indicated that unethical pharmaceutical companies sometimes pay a commission to physicians for recommending more expensive broader spectrum medications when cheaper narrow spectrum alternatives would suffice, resulting in a smaller, highly priced pool of antibiotics for a larger spectrum of infectious diseases[1,2].

Antimicrobial agents are among the most frequently prescribed and inappropriate uses of these agents are associated with the development of antimicrobial resistance. Antibiotics are, frequently prescribed inappropriately in terms of type, dose, duration and indication. Despite the improved trend of health care in Bangladesh, infectious diseases remain priority public health problem, where widespread use of different antimicrobials against bacterial, fungal, viral and parasitic infections is required. Most antimicrobials are prescribed, with the decision to apply based on best-guess empiric therapy. A majority of the prescribers in Bangladesh diagnose infection by clinical assessment and suspect a microbial aetiology. Choosing an antimicrobial to which the infecting organism is susceptible means a shorter delay in starting effective treatment and a lower risk of poor outcomes and prolonged hospital stays, with their associated costs.

The excessive and inappropriate use of antibiotics adds in an unnecessary economic burden to healthcare system and coincides with an increase in drug resistant organisms, which has resulted in the use of more expensive and toxic drugs. It is known that patients infected with drug-resistant organisms are more likely to require hospitalization, have a longer hospital stay and die. It is clear that antibiotic resistance is increasing worldwide and common pathogenic bacteria have become increasingly resistant to useful antimicrobials. The widespread and inappropriate use of antibiotic results in the development of a progressively antibiotic-resistant microbial ecosystem in Bangladesh. This is clearly indicated by the high prevalence of antibiotic resistance among community acquired *Shigella*, *Salmonella*, *Vibrio cholerae*, *Escherichia coli*, *Neisseria gonorrhoe*, *Mycobacterium tuberculosis*, *Sptreptococcus pneumonia* and *Heamophilus influenza* infections in Bangladesh[3].

Materials & Methods

This is an observational (retrospective) cross sectional type of study. The study was conducted at Armed Forces Institute of Pathology, Dhaka by reviewing the register which contains detail record of culture and sensitivity of different samples. All of the samples of urine (173), Blood (31), pus (63), sputum (28) and throat swab (14) tested for culture and sensitivity in that centre over a period from January 2012 to February 2013 were included in this study. Selected antibiotics were ciprofloxacin, cephradine and cefixime. Data were analyzed by using software IBM SPSS Statistics 19.0.

Result

In this study there are five different types of samples are considered. These are urine, blood, pus, sputum and throat swab. Total numbers of different samples were- Urine (173), Blood (31), Pus (63), Sputum (28) and Throat swab (14). The study reveals the common organisms present in different samples and their sensitively to three selected antibiotics which are commonly used in practice. Diagram-1 shows the organisms isolated from urine, where *E.coli* is 100 (57.8%) most frequent,

followed by *Klebsiella* 31 (17.9%) and *Acinetobacter* is 18 (10.4%). Among these *Acinetobacter* is highly capable of mutation thus develops resistance to antibiotics.

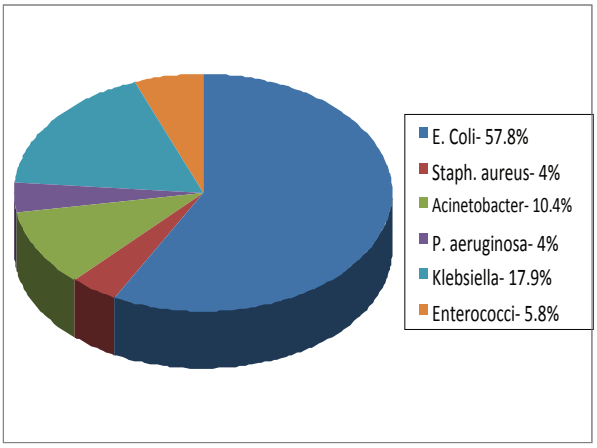

Diagram-1: Organisms of urine.

Table-I shows the susceptibility of three selected antibiotics (Ciprofloxacin, Cephradine and Cefixime) to organisms of urine. Organisms were highly resistant to Cephradine (95%) and Cefixime (69.6%). But to ciprofloxacin which is widely used in cases of UTI in our country were found 72.8% resistant.

Table-I: Sensitivity of organisms isolated from urine to antibiotics.

Name of Antibiotics	Sensitive	Resistant	Total
Ciprofloxacin	27.2% (47)	72.8% (126)	173
Cephradine	5.0% (8)	95.0% (153)	161
Cefixime	30.4% (51)	69.6% (117)	168

Diagram-2 shows organisms isolated from blood. Here the frequency of *S.typhi* was 17 (54.9%) and *S. Paratyphi* 8 (25.8%).

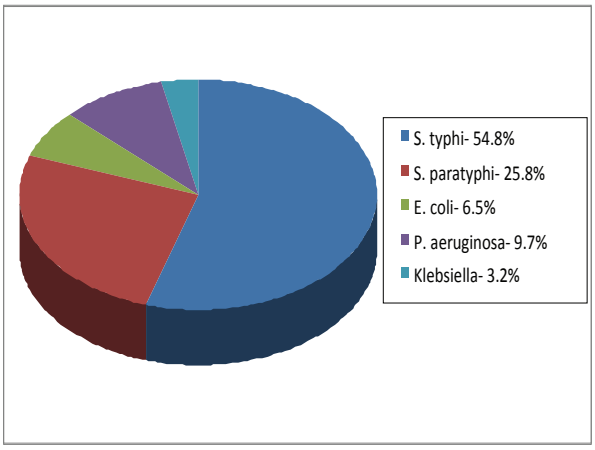

Diagram-2: Organisms isolated from blood.

Organisms from blood were highly sensitive to both cefixime and ciprofloxacin (Table-II). Organisms were 83.3% and 80.6% sensitive to cefixime and ciprofloxacin respectively whereas they were mostly resistant to cephradine (65.4%).

Table-II: Sensitivity of organisms isolated from blood to antibiotics.

Name of Antibiotics	Sensitivity	Resistance	Total
Ciprofloxacin	80.6% (25)	19.4% (6)	31
Cephradine	34.6% (9)	65.4% (17)	26
Cefixime	83.3% (25)	16.7% (5)	30

Diagram-3 shows total 63 samples of pus examined. Among the organisms *staph. aureus* was 27(42.9%), *E.coli* 18(28.6%) and *Acinetobacter* 10(15.9%). Beside Pus, presence of *Acinetobacter* is also noticeable in urine (10.4%).

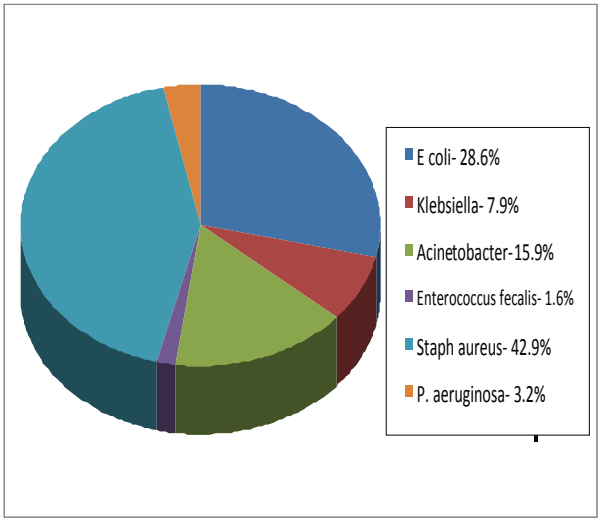

Diagram-3: Organisms of pus.

Organisms of pus were highly resistant to all three selected antibiotics (Table-III).

Table-III: Sensitivity of organisms isolated from pus to antibiotics.

Name of Antibiotics	Sensitive	Resistant	Total
Ciprofloxacin	36.5% (23)	63.5% (40)	63
Cephradine	17.5% (11)	82.5% (52)	63
Cefixime	24.2% (15)	75.8% (47)	62

Presence of organisms in sputum are shown in Diagram-4. *Klebsiella* 19 (67.8%) was most frequent in sputum followed by *Acinetobacter* (14.3%) and *Pseudomonas aeruginosa* (10.7%).

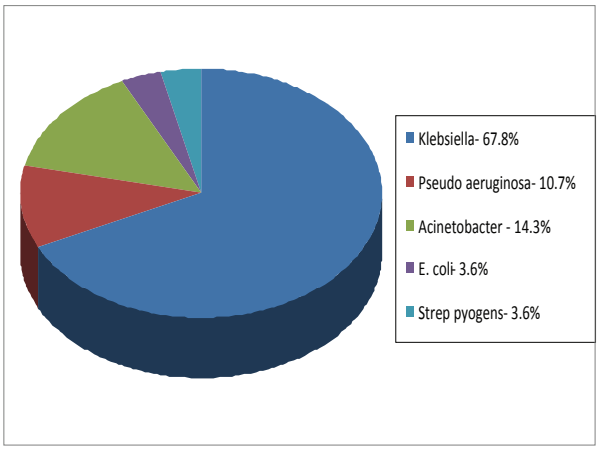

Diagram-4: Organisms isolated from sputum.

Organisms of sputum were highly resistant to both cephradine (92.9%) and ciprofloxacin (75.8%). But to cefixime they were moderately sensitive (64.3%) (Table-IV).

Table-IV: Sensitivity of organisms isolated from sputum to antibiotics.

Name of Antibiotics	Sensitivity	Resistance	Total
Ciprofloxacin	24.2% (20)	75.8% (8)	28
Cephradine	7.1% (2)	92.9% (26)	28
Cefixime	64.3% (18)	35.7% (10)	28

Among the Organisms of throat swab *streptococcus pyogens* were highly frequent 11 (78.6%) out of total 14 samples which is illustrated in Diagram-5. Others are *klebsiella* (14.3%) and *Staph aureus* (7.1%).

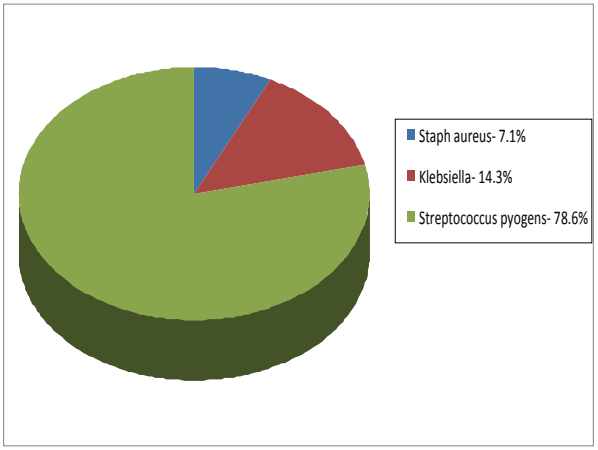

Diagram-5: Organisms isolated from throat swab.

Unlike other samples organisms were found moderately sensitive to cephradine (71.4%) in throat-swab isolates. On the other hand susceptibility of cefixime (42.9%) and ciprofloxacin (50%) were almost same (Table-V).

Table-V: Sensitivity of organisms isolated from throat swab to antibiotics.

Name of Antibiotics	Sensitive	Resistant	Total
Ciprofloxacin	50.0% (7)	50.0% (7)	14
Cephradine	71.4% (10)	28.6% (4)	14
Cefixime	42.9% (6)	57.1% (8)	14

Discussion

The study was conducted in Armed Forces Institute of Pathology to assess the current state of antimicrobial resistance of different samples mainly among the Armed Forces personnel. The aim of the study was to reveal the real picture of antimicrobial resistance in our country. Antibiotic resistance has increased dramatically and rapidly during 1990s and it is widely acknowledged to a serious threat to the treatment of infective diseases on a global basis. The spread of antibiotic resistance presents a major public health challenge for the future. There are clinical data and study are available in this particular field showing that treatment of bacterial infections with antibiotics to which the infecting pathogen is resistant is associated with morbidity, mortality and cost.

In this study five different types of samples were considered (Urine, blood, pus, sputum and throat swab) to identify common microorganisms and to assess their sensitivity to three selected antibiotics. In this study the organisms isolated from urine were *E.coli* 57.8%, *Klebsiella* 17.9%, *Acinetobacter* 10.4%, *Pseudomonas* 4% and others 9.8%. Whereas a study conducted at Stamford University, Bangladesh shows organisms isolated from urine were *E.coli* 66.92% followed by *Klebsiella spp.* 13.45%, *Proteus* 6.77% and *pseudomonas* 6.77%[4]. These results of two different studies both conducted in Bangladesh shows similar outcome.

A study conducted in Ankara, Turkey showed *E. coli* was the causative agent in 90% of uncomplicated UTIs and in 78% of the complicated UTIs[5]. Our study shows the rate of resistance of the isolates from urine to cephradine 95%, ciprofloxacin 72.8% and cefixime 69.6%. Another study conducted at Armed Forces institute of Pathology showed resistance of the organisms of urine to ciprofloxacin 83.93% and to cefixime 71.43%[6]. A study conducted in Bangladesh reveals that *E.coli* was resistant in 40% of cases to commonly used antibiotics (e.g. ceftriaxone, ciprofloxacin etc) and 95% resistant to azithromycin[7]. *Klebsiella pneumoniae* also showed similar pattern[8]. A Study conducted in UK and lreland shows ESBL producing *E.coli* were very commonly multidrug resistant, with 83% showing ciprofloxacin non- susceptibility. A study in Turkey showed organisms isolated from respiratory and urinary tracts were *Pseudomonas* (26.8%), *Kelbsiella* (26.2%), *E.coli. Acinetobacter* and *Enterobacter* which were also found in our samples but there were differences in frequency of organisms[9]. Another study in Karachi, Pakistan reveals Klebsiella isolates from urine was sensitive to cefuroxime 55.9%, cefixime 57.7%, and to ciprofloxacine 62.5%[10].

Our study shows organisms isolated from blood were *S.typhi* 54.8%, *S. paratyphi* 25.8%, *Pseudomonas* 9.7%, *E.Coli* 6.5% and *Klebsiella* 3.2%. A study in Combodia shows blood culture isolates were *S. cholerasuis* 51.4% and *S.typhi* 27.8% which shows a significant difference with our study[11]. Organisms isolated from blood shows resistance to ciprofloxacin 19.4%, cefixime 16.7% and to cephradine 65.4% in this study. Another study conducted in India shows resistance of *S.typhi* to ciprofloxacin is 4.21% to 6.31% of the total 322 isolates 57.8% *S. typhi* were sensitive to ciprofloxacin in a study conducted in a tertiary care hospital in southern India[12]. All the study shows a wide range of variation. Organisms isolated from pus were *S.aureus* 42.9% *E.coli* 28.6%, Acinetobacter 15.9% and *Klebsiella* 7.9% in this study. Whereas in another study conducted in AFIP,Dhaka shows 38.38% isolated organisms of pus were Pseudomonas. Resistances of organisms of pus to different antibiotics were ciprofloxacin 63.5%, cephradine 82.5% and cefixime 75.8%. In a study conducted at AFIP shows almost a similar result[6]. Here resistance to ciprofloxacin was 61.84% and to cefixime 93.3%.

The study shows organisms isolated from sputum were *Klebsiella* 67.8%, *Acinetobacter* 14.3% and *pseudomonas* 10.7% which is almost same as another study conducted in 2012 at AFIP where *pseudomonas* was found 10%. Organisms of sputum were highly resistant to both cephradine (92.9%) and ciprofloxacin 75.8% but to cefixime they were found mostly sensitive (64.3%). A study in India shows *Klebsiella* were highly sensitive to *quinolone* (85%) but to cephalosporin (Ceftizoxime and cefotaxime) they were found 28% to 76% resistance. In another study from Gwalior, India reveals most of the *klebsiella* are multidrug resistance. A study in USA, 1998-2010 demonstrated significant increases in antimicrobial resistance of *Klebsiella*. The largest increases in antimicrobial drug resistance from 1998 to 2010 were observed for Aztreonam (7.7% to 22.2%), ceftazidime (5.5% to 17.2%), and ciprofloxacine (5.5% to 16.8%). There is three to four fold rise of antimicrobial resistance in USA over a decade which is even much lower than our country[13].

In our study organisms isolated from throat swab were *streptococcus pyogenes* 78.6% followed by *Klebsiella* 14.3% and *S. aureus* 7.1%. A study in Benin reveals common organisms of throat swab were *streptococcus pyogenes* 48.72%, *S. aureus* 12.83% and *Klebsiella* 17.9%[14], both studies reveal similar organisms on throat swab culture. In our study organisms of throat swab were found moderately sensitive to cephradine (71.4%). But to cefixime and ciprofloxacin they were less sensitive 42.9% and 50% respectively. A study in Berlin, Germany showed Streptococcus pyogens isolated from throat swab was 2.8% resistant to ciprofloxacin and erythromycin were 10.7% to 18.9% respectively. Another study in Lebanon in 2010 revealed *Streptococcus pyogens* were 10%

resistant to erythromycin and 3% to both erythromycin and clindamycin, both the study shows remarkable less number of resistant cases than in our study[15]. Surveillance in Taiwan shows high rates of non susceptibility of *streptococcus* to penicillin 60%, cefaclor 67%, cefuroxime 62%, cefpodoxime 64% etc[16]. A retrospective study by Delhi hospital over 77,000 patients admitted in between 2000-2009 found a rise in antibiotic resistance by 40%-97% with increased prescription of drugs[17].

It is clearly evident from our study that antimicrobial resistances to commonly used antibiotics were much higher than our expectation. Organisms were highly resistant (72.8%) to ciprofloxacin which is commonly used by our physician to treat UTI. In case of organisms of blood both ciprofloxacin (80.6%) and cefixime (83.3%) showed very good sensitivity. Organisms of pus were highly resistant to all the three antibiotics used in the study. On the other hand organisms of sputum were also found mostly resistant to antibiotics. Organisms isolated from throat swab showed better sensitivity to cephradine (71.4%) than cefixime (42.9%) and ciprofloxacin (50%). The study showed the organisms of different samples were highly resistant to commonly used antibiotics even to third generation cephalosporins. Antibiotics become less effective against micro-organisms because of their indiscriminate, misuse, and over prescription by the physicians, non compliance of the patients, lack of awareness and lack of proper monitoring. Strict compliance of policy on drugs and continuous monitoring and surveillance may revert the current alarming situation of antimicrobial resistance in our country.

Conclusion

The study reveals a grave picture regarding the antimicrobial resistance in our country. The result may vary in the perspective of whole country as the study conducted at AFIP. Here most of the samples were collected from CMH, Dhaka which is the only referral hospital of Bangladesh Armed Forces and the cases were usually complicated. There is no estimation about the actual cost of antimicrobial resistance in our country. But certainly it is a huge socio-economic burden for the countries like Bangladesh. According to the Centre for Disease Control and Prevention(CDC), antibiotic resistance in the United States costs an estimated $ 20 billion a year in excess health care costs, $ 35 million in other societal costs and more than $ 8 million additional days that people spend in the hospital(April 2011).

The irrational and inappropriate uses of antibiotics are the main culprit for the development of resistance of different species of microorganisms to antibiotics. There is an urgent need to develop and strengthen antimicrobial policy (which includes regulations of marketing, sales, use and consumption of these drugs), standard treatment guidelines and national plan for containment of antimicrobial resistance in Bangladesh. There should be more focus on surveillance and research related to public health aspects of antimicrobial resistance at community and hospital level.

References

1. Rosy Reynolds, Antimicrobial resistance in the UK and Ireland, Journal of Antimicrobial Chemotherapy (2009), Suppl. 1, i19-i23 Doi: 10.1093/jac/dkp257.

2. John M Conly, B Lynn Johnston, Antibiotic resistance in Canada at the dawn of the new millennium - A model for the developed world, Canada Journal of Infectious Disease, 2000 Sep-Oct; 11(5): 232–6.

3. Rahman M, Rahman ATMA,The growing antibiotic resistance, a crisis needs rational use of antibiotics, The ORION Vol. 1 September 1998.

4. Farjana Rahman, Sadia Chowdhury, Md Majibur Rahman, Dilruba Ahmed, Anowar Hossain, Antimicrobial Resistance Pattern of Gram-negative Bacteria Causing Urinary Tract Infection, Stamford Journal of Pharmaceutical Sciences > Vol 2, No 1 (2009).

5. Hande Arslan1, özlem Kurt Azap1, önder Ergönül2 and Funda Timurkaynak1 on behalf of the Urinary Tract Infection Study Group, Risk factors for ciprofloxacin resistance among Escherichia coli strains isolated from community-acquired urinary tract infections in Turkey, Journal of Antimicrobial Chemotherapy (2005) 56, 914-8.

6. Khisa S. Antibiotic resistance pattern of Pseudomonas aeruginosa isolates from different specimens received at AFIP,Dissertation,P65-79.

7. Lina TT, Rahman SR, Gomes DJ. Multiple-antibiotic resistance mediated by plasmids and integrons in uropathogenic Escherichia coli and klebsiella pneumonia-Bangladesh. Journal of Microbiology. 2007;24(1):19-23.

8. Rahman MM, Haq JA, Hossain MA,Sultana R, Islam F, Islam A.H.M.S. Prevalence of extended-spectrum-lactamase-producing Escherichia coli and klebsiella pneumonia in an urban hospital in Dhaka Bangladesh. International Journal of Antimicrobial Agents. 2004;24:508-10.

9. Filiz Günserena, Latife Mamiko Süheyla Öztürkb, Mine Yücesoy, Kadir Bibero Nuran Yulu Mehmet Do Sesin Kocagöze, Serhat Ünale, S1la Cetinf, Semra Calanguf, ìftihar Köksalg, Hakan Leblebicio and Murat Günaydinh,A surveillance study of antimicrobial resistance of Gram-negative bacteria isolated from intensive care units in eight hospitals in Turkey, Oxford journals>Medicine>Journal of Antimicrobial Chemotherapy>Vol43, Issue 3>P373-8.

10. Abdullah FE, Mushtaq A, Irshad M, Rauf H, Afzal N, Rasheed ACurrent efficacy of antibiotics against Klebsiella isolates from urine samples – a multi-centric experience in Karachi, Pak J Pharm Sci. 2013 Jan;26(1):11-5.

11. Erika R. Vlieghemail, Thong Phe, Bigrit De Smet, Chhun H. Veng, Chun Kham, Sophie Bertrand, Raymond Vanhoof, Lut Lynen, Willy E. Peetermans, Jan A. Jacobs, Azithromycin and Ciprofloxacin Resistance in Salmonella Bloodstream Infections inCambodian Adults.(http://www.plosntds.org/article/info%3Adoi%2F10.137%Fjournal.pntd.0001933).

12. Ashwini Choudhary, Ram Gopalakrishnan, Nambi P. Senthur, V. Ramasubramanian, K. Abdul Ghafur, and M.A. Thirunarayan, Antimicrobial susceptibility of Salmonella enterica serovars in a tertiary care hospital in southern India, Indian J Med Res. 2013 April; 137(4): 800–2.

13. Guillermo V. Sanchez, Ronald N. Master, Richard B. Clark, Madiha Fyyaz, Padmaraj Duvvuri, Gupta Ekta, and Jose Bordon, Klebsiella pneumoniae Antimicrobial Drug Resistance, United States, 1998–2010, EID journal Volume 19, Number 1—January 2013.

14. Arvanda Mardjan, Hoeckb Marlies, Hahna Helmut and Wagnera Jutta, Antimicrobial resistance in Streptococcus pyogenes isolates in Berlin, Journal of Antimicrobial Chemotherapy Volume 46, Issue 4Pp. 621-4.

15. Bahnan W, Hashwa F, Araj G, Tokajian S., emm typing, antibiotic resistance and PFGE analysis of Streptococcus pyogenes in Lebanon, J med microbiol 2011 Jan;60(Pt 1):98-101. doi: 10.1099/jmm.0.023317-0.

16. Hsueh PR, Huang WK, Shyr JM, Lau YJ, Liu YC, Luh KT,Multicenter surveillance of antimicrobial resistance of Streptococcus pyogenes, Streptococcus pneumonia, Haemophilus influenzae, and Moraxella catarrhalis to 14 oral antibiotics, J Formos Med Assoc. 2004 sep;103(9):664-70

17. Chatterjee P, Drug resistance: 10 year study shows big jump, New Delhi,Tue Jul 24 2012.(http://www.indianexpress.com/news/drug-resistance-10yr-study-shows-big-jump/978583/).