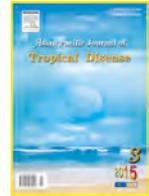




Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Disease

journal homepage: www.elsevier.com/locate/apjtd



Document heading

doi: 10.1016/S2222-1808(14)60662-9

© 2015 by the Asian Pacific Journal of Tropical Disease. All rights reserved.

An epidemiological study on the drug resistance of *Escherichia coli* strains isolated from women patients with urinary tract infection in Shalamzar, Iran

Gholamreza Farnoosh¹, Mohamadreza Mahmoudian Sani², Kazem Hassanpour³, Mostafa Mellat⁴, Ramezan Ali Taheri^{4*}

¹Applied Biotechnology Research Centre, Baqiyatallah University of Medical Sciences, Tehran, Iran

²Department of Parasitology and Mycology, Hamedan University of Medical Sciences, Hamedan, Iran

³Medical School, Sabzevar University of Medical Sciences, Sabzevar, Iran

⁴Nanobiotechnology Research Centre, Baqiyatallah University of Medical Sciences, Tehran, Iran

PEER REVIEW

Peer reviewer

Dr. Mehdi Ghamgosha, Jahrom University, Iran.

Tel: 02177105010

E-mail: Mehdighamgosha@yahoo.com

Comments

This study is useful in which the authors investigate drug resistance of various strains of *E. coli* bacteria isolated from female patients with UTIs in South West of Iran. The current research was conducted for the first time in this region (Shalamzar). From this study, it revealed that there were many factors leading to drug resistance such as prescription of antibiotics without evaluating sensitivity, indiscriminate prescription of antibiotics by doctors without ultimate diagnosis of the infectious agent and intractable antibiotic use by people. So it is important to use sensitivity pattern for health care systems.

Details on Page 244

ABSTRACT

Objective: To investigate drug resistance of various strains of *Escherichia coli* (*E. coli*) bacteria isolated from female patients with urinary tracts infections (UTIs) in Shalamzar, Iran.

Methods: This study was conducted from April 2011 to April 2012 on 150 female patients with positive urine culture and 10^5 CFU/mL colony count. The pattern of antibiotic sensitivity was recognized using antibiogram by the disc diffusion method.

Results: The results revealed that the predominant bacterium was *E. coli* (90%), followed by *Klebsiella pneumonia* (3%). Trimethoprim–sulfamethoxazole is the initial medicine to treat UTIs (without complications) which demonstrated relatively poor activity against *E. coli* (with 40% sensitivity), though alternative medicines such as nitrofurantoin (97% sensitivity) and ciprofloxacin (91% sensitivity) showed good activity against *E. coli* as well.

Conclusions: The findings emphasized the necessity of pursuing the investigations in national and local governments in order to retain the efficacy of treating UTIs using effective antibiotics.

KEYWORDS

Drug resistance, Urinary tract infections, Anti-bacterial agents, Sensitivity, Shalamzar

1. Introduction

Urinary tract infection (UTI) is defined as the presence of significant numbers of pathogenic bacteria, or other organisms, in the urinary system[1]. UTIs are among the most common bacterial diseases worldwide that can be presented

asymptomatic or symptomatic, characterized by a wide spectrum of symptoms ranging from mild irritative voiding to bacteremia, sepsis, or even death. Fifty percent of all women will experience at least once UTI in their lifetime and about 25% of them will have one or more recurrent infections[2]. In latter decades, widespread utilization

*Corresponding author: Ramezan Ali Taheri, Nanobiotechnology Research Centre, Baqiyatallah University of Medical Sciences, Tehran, Iran.

Tel: +98-2182482562

Fax: +98-2188068924

E-mail: taheri@bmsu.ac.ir

Foundation Project: Supported in part by grant from health center of Shahrekord. (Grant No. 3452/55).

Article history:

Received 16 May 2014

Received in revised form 25 May, 2nd revised form 27 May, 3rd revised form 5 Jun 2014

Accepted 30 Jun 2014

Available online 29 Jul 2014

of antibiotics has resulted in the increase incidence of antibiotic resistance among urinary tract pathogens all over the world[3,4].

UTIs is one of the people's health problems in all age groups all over the world[5]. UTIs annually infect about millions of individuals and impose million dollars on health care systems[4,6]. Approximately one third women will require antimicrobial treatment for UTI before 24 years of age, and 40% to 50% of women will have UTI during their lifetime. UTIs in male patients are considered complicated. *Escherichia coli* (*E. coli*) is the most common cause of UTIs[7,8]. Furthermore, about 20% to 40% of women experience an infection relapse seemingly due to the emergence of UTIs antibacterial resistance. Increasing rates of resistance among bacterial uropathogens has caused growing concerns in both developed and developing countries[9]. The pathogenicity depends on the expression of an array of virulence factors produced by *E. coli*. Toxigenic strains of *E. coli* are primarily of three types: enterotoxigenic *E. coli* (ETEC), Shiga toxigenic *E. coli* (STEC) and necrotoxicogenic *E. coli* (NTEC)[10]. Apparently, the medical community around the world has failed to solve the threatening problem of antibiotic resistance growth for which a significant reason is the inappropriate use of antibiotics. Suitable data on the patterns of drug sensitivity may help health authorities to select appropriate antibiotics for patients while providing the researchers with control over the epidemic patterns of antibiotic resistance across the city. The determination of sensitivity patterns is significant in that antibiotic-resistant patterns differ geographically[11–13]. The bacterial resistance may be the effect of antibiotic overuse and self-medication. The purpose of this study was to examine the drug resistance of various strains of *E. coli* bacteria isolated from female patients with UTIs in Shalamzar. Data analysis can examine the sensitivity of such bacteria to antibiotics, consequently investigating their sensitivity in different populations which may lead to reasonable selection of antibiotics for UTIs in the city[14].

2. Materials and methods

All women with positive results for *E. coli* culture in primary tests were referred to Central Laboratory of Shalamzar. In the laboratory, each sample was cultured in three different mediums including blood agar, Eosin Methylene blue and MacConkey's agar and incubated for 24 h at 37 °C. One hundred and fifty strains of bacteria were isolated from 500 cultured samples (90% *E. coli*; 135 strains). All suspected colonies were detected through colony morphology, Gram staining, catalase positivity, oxidase negativity and other biochemical reactions. Patients' information and features and their treatment procedures were recorded in the lab's computer. The study was conducted in a one-year period, from April 2011 to April 2012. The pattern of antibiotic sensitivity was recognized using antibiogram by the disc diffusion method. Bacteria were divided in three classes as high sensitive, moderate

sensitive and resistant. The classification was performed according to National Committee for Clinical Laboratory Standards[15]. The control sample to determine the bacterium sensitivity was *E. coli* ATTC 25922.

3. Results

The predominant isolated bacterial species were *E. coli* which approximately constituted 90% percent of total isolations followed by 3% *Klebsiella pneumoniae*. The rest frequency of isolated bacteria were *Enterococcus* spp.(2%), coagulase-negative *Staphylococci* (2%), *Staphylococcus saprofiticus* (1.8%), *Proteus mirabilis* (1%), *Citrobacter* spp. (0.6%) and *Enterobacter* spp. (0.6%). Trimethoprim-sulfamethoxazole (TMP-SMZ) which was the first line of treatment for urinary infections had little effect on isolated *E. coli* (40% sensitivity). In addition alternative medicines such as ciprofloxacin and nitrofurantoin demonstrated good effects against *E. coli* (91%–97% sensitivity). All samples were highly sensitive to nitrofurantoin and ciprofloxacin, moderately sensitive to TMP-SMZ, gentamicin, cefazolin and tetracycline and were resistant to ampicillin and penicillin. Fluoroquinolones was successfully applied from 2011 to 2012 for curing patients; all 150 patients with positive culture and 10⁵ CFU/mL colony count were cured by fluoroquinolones. Individuals' age range were 18–40 and age distribution was as follows: 45.3% of patients were 18–22 years old, 4.7% were 22–25 years old and 50% were between 25–40 years old. Nearly all colonies were resistant to ampicillin and penicillin and only 40% of the *E. coli* colonies were sensitive to TMP-SMZ and the highest sensitivity of isolated *E. coli* colonies (97%) was against nitrofurantoin.

4. Discussion

The current research was conducted for the first time in this region (Shalamzar) and apparently there had been problems which caused the drug resistance including the lack of clinical diagnostic laboratories in the past years, which led to prescription of antibiotics without evaluating sensitivity, indiscriminate prescription of antibiotics by doctors without ultimate diagnosis of the infectious agent and intractable antibiotic use by people. The majority of clients were from near villages. The reason why they took antibiotics intractably was the lack of knowledge of the side effects and risks of drug resistance; and the lack of full insurance coverage caused them not to visit the doctor. All isolated bacteria were resistant to ampicillin and penicillin, though 60% of them showed resistance to TMP-SMZ, which may be a serious alarm for indiscriminate use of this medicine. A study in Minnesota, USA revealed that *E. coli* resistance to TMP-SMZ was higher in samples than controls, i.e. resistance to this medicine[16]. Another study in Norway endorsed *E. coli* resistance to fluoroquinolones and TMP-SMZ and also resistant genes were explored[17]. The resistance in this area was associated with risk factors such as medicine

overselling and excessive self-medication. In this area, ampicillin, ciprofloxacin and TMP-SMZ are easily provided and used. Moreover according to topics published by the society of infectious diseases, TMP-SMZ is the first without-complications-medicine in UTIs treatment[18]. Therefore self-medication with such medicine provides resistance. Recent published studies confirm that resistance to TMP-SMZ in parts of the world is increasing; furthermore the present study also endorses the situation, such that 60% of patients were resistant to this medicine[19–22]. Our results imply that taking TMP-SMZ is not so specific to this area and alternative medicines (fluoroquinolones and nitrofurantoin) recommended by Infectious Diseases Society of America to cure UTIs can be used. Fluoroquinolones were examined in the present study (ciprofloxacin) to which *E. coli* demonstrated high sensitivity. In addition, nitrofurantoin revealed such sensitivity as well such that 97% of *E. coli* strains were highly sensitive. In a study, Sangeeth *et al.* concluded that the increased resistance to fluoroquinolones in *E. coli* could be due to its inappropriate usage[23]. It is imperative to rationalize the use of fluoroquinolones in order to prevent the dissemination of resistant strains in the population[23].

UTIs are normally due to bacterial infections which may occur during a person's life. Unfortunately most of the treatments begin to be prior to the results of the culture; as a consequence the results of the sensitivities differ with the previous studies. Therefore the study of resistance among uropathogens is important to prescribe appropriate medicine and to prevent indiscriminate prescription in order to decline the medical resistance. Such studies can be useful for determining the risk factors of bacterial resistance[24]. Increasing occurrence of multiple β -lactamases in clinical isolates could lead to therapeutic failure. Hence, early detection of β -lactamase production can benefit implementation of proper antibiotic therapy and infection control policies[25].

In similar work, Jalilian *et al.* confirms that *E. coli* is still the most common isolated uropathogen[26]. Augmentin and amikacin are not as a first choice for treatment of UTI in Kermanshah Area. Ampicillin and nitrofurantoin may be considered as the first choice empiric agent to out-patients.

In a study, Thiraviam *et al.* concluded that a high number of *E. coli* strains isolated from both diabetic and non diabetic patients showed resistant to the antibiotic rifampicin and ciprofloxacin[27]. However, the resistant to rifampicin was more than the ciprofloxacin. The representative isolates lost their antibiotic resistance after curing hence it was inferred that the antibiotic resistant was plasmid borne.

Further investigation in national levels and preventive measures for medical resistance are required. Further research should be directed on determining the resistant strains of bacteria, their polymorphism, and epidemiology and how they spread; inattention to resistance mechanisms, spread and degree of prevalence may hinder treatment of bacterial infections and medicines intractable use[28].

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

The authors wish to thank manager and staff of Central Laboratory of Shalamzar for conducting sampling, culturing and some laboratory tests of specimens. This study was supported in part by grant from health center of Shahrekord. (Grant No. 3452/55).

Comments

Background

Investigating bacterial sensitivity patterns of uropathogens in national and local levels provides significant data regarding the emergence of antibiotic resistance issues in order to help health management system. The aim of this study was to investigate drug resistance of various strains of *E. coli* bacteria isolated from female patients with UTIs in South West of Iran.

Research frontiers

UTIs arouse people's health problems in all age groups all over the world. UTIs annually infect about millions of individuals and impose million dollars on health care systems. Thus defining bacterial sensitivity pattern of women with UTIs is very important for health care systems.

Related reports

Jalilian *et al.* confirms that *E. coli* is still the most common isolated uropathogen. Augmentin and amikacin are not as a first choice for treatment of UTI in Kermanshah area. Thiraviam *et al.* concluded that a high number of *E. coli* strains isolated from both diabetic and non diabetic patients showed resistant to the antibiotic rifampicin and ciprofloxacin.

Innovations & breakthroughs

The acquired results implicate sensitivity of isolated bacteria to antibiotics, investigating their sensitivity in different populations which may lead to good selection of antibiotics for UTIs in region of study.

Applications

Epidemiological results of bacterial sensitivity pattern of women with UTIs are very significant for drug medication and prevention.

Peer review

This study is useful in which the authors investigate drug resistance of various strains of *E. coli* bacteria isolated from female patients with UTIs in South West of Iran. The current research was conducted for the first time in this

region (Shalamzar). From this study, it revealed that there were many factors leading to drug resistance such as prescription of antibiotics without evaluating sensitivity, indiscriminate prescription of antibiotics by doctors without ultimate diagnosis of the infectious agent and intractable antibiotic use by people. So it is important to use sensitivity pattern for health care systems.

References

- [1] Ngwai YB, Iliyasu H, Young E, Owuna G. Bacteriuria and antimicrobial susceptibility of *Escherichia coli* isolated from urine of asymptomatic university students in Keffi, Nigeria. *Jundishapur J Microbiol* 2012; **5**(1): 323–327.
- [2] Giray B, Uçar FB, Aydemir SŞ. Characterization of uropathogenic *Escherichia coli* strains obtained from urology outpatient clinic of Ege Medical Faculty in İzmir. *Turk J Med Sci* 2012; **42**(Suppl 1): S1328–S1337.
- [3] Mirzarazi M, Rezatofighi SE, Pourmahdi M, Mohajeri MR. Antibiotic resistance of isolated Gram negative bacteria from urinary tract infections (UTIs) in Isfahan. *Jundishapur J Microbiol* 2013; **6**(8): e6883.
- [4] Khoshbakht R, Salimi A, Aski HS, Keshavrzi H. Antibiotic susceptibility of bacterial strains isolated from urinary tract infections in Karaj, Iran. *Jundishapur J Microbiol* 2012; **6**(1): 86–90.
- [5] Orenstein R, Wong ES. Urinary tract infections in adults. *Am Fam Physician* 1999; **59**: 1225–1234.
- [6] Foxman B, Barlow R, D'Arcy H, Gillespie B, Sobel JD. Urinary tract infection: self-reported incidence and associated costs. *Ann Epidemiol* 2000; **10**: 509–515.
- [7] Kunin CM. Urinary tract infections in females. *Clin Infect Dis* 1991; **18**: 1–10.
- [8] Amin M, Mehdinejad M, Pourdangchi Z. Study of bacteria isolated from urinary tract infections and determination of their susceptibility to antibiotics. *Jundishapur J Microbiol* 2009; **2**(3): 118–123.
- [9] Gupta K. Addressing antibiotic resistance. *Dis Mon* 2003; **49**: 99–110.
- [10] Rahman H, Deka M. Detection & characterization of necrotoxin producing *Escherichia coli* (NTEC) from patients with urinary tract infection (UTI). *Indian J Med Res* 2014; **139**: 632–637.
- [11] Ikaheimo R, Siitonen A, Heiskanen T, Kärkkäinen U, Kuosmanen P, Lipponen P, et al. Recurrence of urinary tract infection in a primary care setting: analysis of a 1-year follow-up of 179 women. *Clin Infect Dis* 1996; **22**: 91–99.
- [12] Bajaj JK, Karyakarte RP, Kulkarni JD, Deshmukh AB. Changing aetiology of urinary tract infections and emergence of drug resistance as a major problem. *J Commun Dis* 1999; **31**: 181–184.
- [13] Dyer IE, Sankary TM, Dawson JA. Antibiotic resistance in bacterial urinary tract infections, 1991 to 1997. *Western J Med* 1998; **169**: 265–268.
- [14] World Health Organization. *WHO global strategy for containment antimicrobial resistance*. Geneva: World Health Organization; 2001.
- [15] Clinical and Laboratory Standard Institute. *Performance standards for antimicrobial susceptibility testing; 16th informational supplement. 14M100–S16*. Pennsylvania: Clinical and Laboratory Standard Institute; 2006.
- [16] Johnson JR, Sannes MR, Croy C, Johnston B, Clabots C, Kuskowski MA, et al. Antimicrobial drug-resistant *Escherichia coli* from humans and poultry products, Minnesota and Wisconsin, 2002–2004. *Emerg Infect Dis* 2007; **13**(6): 838–846.
- [17] Grude N, Strand L, Mykland H, Nowrouzian FL, Nyhus J, Jenkins A, et al. Fluoroquinolone-resistant uropathogenic *Escherichia coli* in Norway: evidence of clonal spread. *Clin Microbiol Infect* 2008; **14**(5): 498–500.
- [18] Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). *Clin Infect Dis* 1999; **29**: 745–758.
- [19] Karlowsky JA, Kelly JL, Thornsberry C, Jones ME, Sahm DF. Trends in antimicrobial resistance among urinary tract infection isolates of *Escherichia coli* from female outpatients in the United States. *Antimicrob Agents Chemother* 2002; **46**: 2540–2545.
- [20] Gordon KA, Jones RN, SENTRY Participant Groups. Susceptibility patterns of orally administered antimicrobials among urinary tract infection pathogens from hospitalized patients in North America: comparison report to Europe and Latin America. Results from the SENTRY Antimicrobial Surveillance Program (2000). *Diagn Microbiol Infect Dis* 2003; **45**: 295–301.
- [21] Gupta K, Sahm DF, Mayfield D, Stamm WE. Antimicrobial resistance among uropathogens that cause community-acquired urinary tract infections in women: a nationwide analysis. *Clin Infect Dis* 2001; **33**: 89–94.
- [22] Huovinen, P. Resistance to trimethoprim-sulfamethoxazole. *Clin Infect Dis* 2001; **32**: 1608–1614.
- [23] Sangeeth K, Rajesh KR, Indrapriyadharsini R. Antibiotic resistance pattern of *Escherichia coli* causing urinary tract infection with an emphasis on fluoroquinolone resistance. 2014. [Online] Available from: <http://www.gjmedph.org/uploads/O3-Vo3No1.pdf> [Accessed on 15th April, 2014]
- [24] Ebrahimzadeh MA, Mahdavee MR, Vahedi M. Antibiotic resistance in *E. coli* isolated from urine: a 2-years study isolated from patient with urinary tract infections in Iran. *J Cell Tissue Res* 2005; **5**(2): 445–448.
- [25] Salimi F, Eftekhari F. Coexistence of AmpC and extended-spectrum β -lactamases in metallo β -lactamase producing *Pseudomonas aeruginosa* burn isolates in Tehran. *Jundishapur J Microbiol* 2013; **6**: e7178.
- [26] Jalilian S, Farahani A, Mohajeri P. Antibiotic resistance in uropathogenic *Escherichia coli* isolated from urinary tract infections out-patients in Kermanshah. *Int J Med Public Health* 2014; **4**: 75–77.
- [27] Thiraviam M, Yadesa D, Adugna T. Antibiotic resistant pattern of urinary tract infection causing *Escherichia coli* isolated from diabetic mellitus and non-diabetic mellitus patients with special to Rifampicin resistance. *Int J Curr Microbiol Appl Sci* 2014; **3**(3): 668–674.
- [28] Moniri R, Khorshidi A, Akbari H. Emergence of multidrug resistant strains of *Escherichia coli* isolated from urinary tract infections. *Iran J Public Health* 2003; **32**(4): 42–46.