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The Prevalence of Asymptomatic Bacteriuria in Long Term Care Facility Residents in Shiraz, Southwest Iran: A Cross-Sectional Study

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Abstract: This study detected the prevalence of Asymptomatic Bacteriuria (ABU) in residents of long term care facilities in Shiraz, Southwest Iran. From 100 residents aged between 55-95 years old, aseptically collected mid-stream urine samples underwent culture and antimicrobial sensitivity analysis. The prevalence rate of ABU was 53% with 95% CI 43.2 to 62.8% which was higher than that for elsewhere. ABU was observed more frequently in the females (57.7%), elderly (89%) and diabetic elderly subjects (72.3%). ABU in the diabetic elderly was also more than that for non-diabetic elderly subjects ($p < 0.05$). *E. coli* was the most common bacteria isolated. Resistance rate of gram positive bacteria to penicillin and cefazolin were 100% and those for tetracycline and vancomycin were 72.2 and 66.7%, respectively. The most gram negative bacteria were sensitive to aminoglycosides. Present results showed a higher prevalence of unknown ABU in the residents of nursing homes in Shiraz, Iran as compared to other countries in the world. It might be due to lack of efficient institutional care and uncontrolled diabetes mellitus or other factors influencing immunity.

Key words: Prevalence, asymptomatic bacteriuria, long term care facility, Shiraz, Iran

INTRODUCTION

Urinary Tract Infections (UTIs) are common in nursing homes and carry significant morbidity and subsequent health care costs. UTI describes a spectrum of disease from bacteriuria to pyelonephritis and can be clinically grouped into symptomatic or asymptomatic (Nicolle, 2000). The definition of Asymptomatic Bacteriuria (ABU) or bacteriuria is controversial as some defined it as the quantitative growth of bacteria, greater than or equal to 10^5 colony forming units per milliliter urine of the same organism, on aseptically collected midstream urine specimens, in the absence of symptoms of urinary tract infection on two or more consecutive occasions (Harding *et al.*, 2002). However, for others a single occasion is sufficient. ABU prevalence is estimated to be about 5% in normal healthy female population (Hooton *et al.*, 2000). It is also a common finding in the subjects confined to bed in hospitals and nursing homes with the rate of 20 to 50% (Nicolle, 2000; O'Donnell and Hofmann-Mary, 2002). The prognostic significance of ABU resides in the observation that persons with ABU in certain medical conditions, such as diabetes mellitus and pregnancy, are at increased risk of pyelonephritis and renal impairment (Stein and Funfstuck, 1999; Hooton *et al.*, 2000).

Many bacteria including *Kelebsiellae*, *Enterobacter*, *Proteus*, *Pseudomonas*, *Stapylococcus saprophyticus*, *Stapylococcus aureus* and *Escherichia coli*, as the mostly reported prevalent ones, are reported to cause UTI (Chon *et al.*, 2001). Antibiotic resistant bacteria such as methicillin-resistant *Staphylococcus aureus*, vancomycin resistant *Enterococcus*, *Clostridium difficile*, extended-spectrum beta-lactamase producing gram negative bacilli, fluoroquinolone-resistant strains of *Salmonella* are also reported in the nursing homes (Safdar and Maki, 2002; Chon *et al.*, 2001; Drinka *et al.*, 2001). UTI is spontaneously arisen by urethral contamination with the stool, but other factors predispose this problem. Factors such as age, sex, urethral and genital problems, diarrhea, having catheter and Immune deficiency, sexual activity, genetics, pregnancy, drug usage, skin infections, diabetes, renal abscess, sickle cell anemia, cancer, chemotherapy, general disability and confinement to bed in hospital are effective (Chon *et al.*, 2001; Nicolle, 2000).

The elderly and disabled people in nursing institutions with significant bacteriuria do not have symptoms and there is no change in the symptom when bacteriuria occurs and abates; however, a positive urine culture in a non-specifically unwell subject may be an incidental finding and leads the clinician away from the true diagnosis (Yates, 1999; Boscia *et al.*, 1986). There is

a consensus that asymptomatic bacteriuria in the elderly does not increase morbidity, or antibiotic therapy does not decrease morbidity but it is usually followed by recurrence of bacteriuria, increasing antimicrobial resistance and adverse effects. However, antibiotics are still frequently used to treat asymptomatic bacteriuria in this population as the presence of ABU provides the potential for symptomatic UTI, acute pyelonephritis or other sequelae. In high risk groups (diabetes, immunocompromised) an increased morbidity exists and with bacteriuria especially in those for whom instrumentation is planned, there is an increased risk of bacteraemia (Walker *et al.*, 2000; Yates, 1999). Nevertheless, as ABU is linked with functional status as quality indicator of institutional care and infection control (Lin *et al.*, 2006) study of its prevalence in different locations is worthy of investigation.

Because of the lack of information about the asymptomatic bacteriuria in our nursing homes, the present study was undertaken to detect the prevalence of asymptomatic urinary tract infection, the bacterial causative agents and the possible antibiotic resistance of isolated bacteria to current antibiotics used, in the residents at four major long term nursing homes in Shiraz, southwest Iran. Possible risk factors of asymptomatic urinary tract infection were also investigated among the subjects of this study.

MATERIALS AND METHODS

This descriptive study was performed on 100 residents at four long term nursing homes (Nikan, Farzanegan, Forough-e-Ferdous and Mehr) from October 1, 2002 to September 30, 2003 in Shiraz, southwest Iran. These are the only major nursing homes having a total number of 158 residents. These nursing homes provide care to the elderly, disabled and some other helpless residents.

After explaining the whole project to the authorities, nurses and all the residents of these nursing homes, informed consent were obtained from the residents or their legal guardians in accordance with the ethical standards of the local ethics committee at Shiraz University. The residents were clinically examined and complete history was taken from all of them. The resident men and women with ABU (i.e., with no dysuria, suprapubic pain, frequency and urgency, fever, chills and flank pain) were included in this study and the patients with urinary catheter of any etiology and renal transplant recipients were excluded. None of the participants was on antibiotic therapy. Aseptically collected midstream urines were obtained from the 100 symptom-free participant of

the study by the staffs of nursing homes and sent for microbiological culture on the same day.

Bacterial culture was performed by streaking 0.002 mL of midstream collected urine with a calibrated loop on MacConkey (Hi media, India) and 5% sheep blood agar (Hi media, India) plates (Streak plate culture method was used to detect bacteria in the urine). These agar plates were incubated at 37°C for 24 h under aerobic conditions. The isolates were considered significant if there was $\geq 10^5$ (cfu mL⁻¹) with an isolates. ABU was considered as an organism which is isolated in quantitative counts of 10^5 colony forming unit/mL (cfu mL⁻¹) or more in two consecutive specimens of urine (Stamm, 1992). The mixed growths, in any count, of two or more than two organisms were considered to be contaminated. Significant isolates were selected for identification and antimicrobial susceptibility testing using routine biochemical testing.

Antimicrobial susceptibility testing was done by Kirby-Bauer's disc diffusion method for all isolated bacteria on Muler-Hinton agar (Hi media, India), to determine their resistance or sensitive pattern against common antibiotics, following National Committee for Clinical Laboratory Services guidelines (NCCLS, 2000).

The demographic information of all the subjects, any underlying infection, was prepared in a questionnaire by referring to each resident's file in the related nursing home. The results were statistically analyzed and the groups were compared by Chi square tests using SPSS (11.5) software. The tests were considered significant if $p < 0.05$.

RESULTS

As shown in Table 1, of a total of 100 participants, 78 (78%) were female and 22 (22%) males with the mean age of 67 (55-95) years old. Pure bacteria were grown in samples of 53 cases or 53% (95% CI, 43.2- 62.8%) with the number of colonies higher than 10^5 mL⁻¹ considered having ABU. 8 (15.1%) subjects with ABU were male and 45 of them (84.9%) were female. The prevalence of ABU in our study was 36.4% in men and 57.7% in women. The mean age of the participants was 67, ranging from 55 to 95 years old. Twenty residents (20%) aged less than 65 years and the rest of them (80%) were over 65 years of age which considered as elderly subjects. 6 (11%) of ABU cases aged 55-65 years vs 47 (89%) older than 65 years old. Of the total 80 elderly residents 47 (59%) showed ABU in our elderly subject showing significantly more ABU cases among the elderly residents as compared to younger ones ($p < 0.05$).

Thirty four of the ABU elderly subjects (72.3%) in this study had the history of diabetes. The prevalence of

Table 1: Distribution of the ABU subjects in nursing homes under study according to age, sex and suffering from diabetes

Age	Male ABU cases		Female ABU cases		Total
	Non-diabetic	Diabetic	Non-diabetic	Diabetic	
<65 (n = 20)	1 (1.9%)	0 (0%)	5 (9.4%)	0 (0%)	6 (11.3%)
>65 (n = 80)	1 (1.9%)	6 (11.3%)	12 (22.6%)	28 (52.8%)	47(88.7%)
Total	8 (15.1%)		45 (84.9%)		53 (100%)

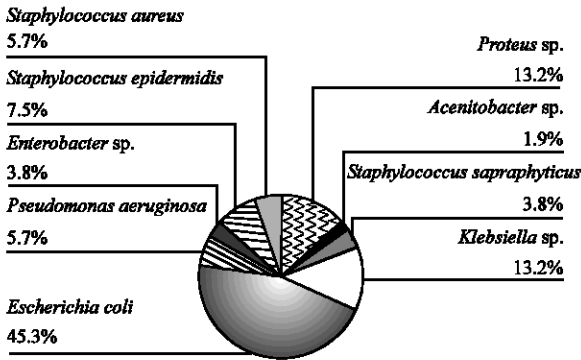


Fig. 1: Prevalence of isolated bacteria from 53 asymptomatic UTI cases out of 100 residents of nursing homes under the study

asymptomatic UTI in this study was more than that for non-diabetic (27.7%) elderly subjects with a ratio of 2.62 and such a difference was significant ($p < 0.05$).

E. coli was the most common bacteria isolated. Of the 53 samples 24 (45.3%) grew *E. coli* in a significant quantity. Other most prevalent bacteria were *Klebsiella*, *Proteus*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Staphylococcus saprophyticus*, *Pseudomonas aeruginosa*, *Enterobacter* and *Acenitobacter*, respectively (Fig. 1). All of these organisms were grown in pure cultures.

All isolated gram positive bacteria were resistant to penicillin, cefazolin (100%), mostly were resistant to tetracycline (72.2%) and vancomycin (66.7%) and co-trimoxazole (56.1%), but all gram positive isolates (100%) were susceptible to ciprofloxacin.

For the recovered gram negative bacteria in our study, high resistance rate was observed against nalidixic acid (85.3%) and co-trimoxazole (52.5%), however; susceptibility rates to minglycosides including amikacin, gentamicin and tobramycin were 91.5, 87.8 and 82.1%, respectively. Most of the gram negatives (88.1%) were sensitive to ciprofloxacin except for one resistant isolate of *Acenitobacter* and 79% of *E. coli* isolates.

DISCUSSION

The prevalence rate of ABU in long term care facility residents was 53% in this study; this rate was higher than that in the healthy population (Hooton *et al.*, 2000; Tencer, 1988). The major determinants of ABU status are

age, gender, genetic factors, antibiotic exposure, functional status and special conditions like diabetes, urinary catheterization (Bonadio *et al.*, 2006; Orrett and Shurland, 2001; Balasoiu *et al.*, 1999). The small number of subjects in this study is a limitation of the present study. This was partly due to the low number of the nursing homes existing in Shiraz and the low number of the residents living there. The consequence of having a small numerator is that the precision of our prevalence estimate is affected and this is reflected in a wide 95% confidence interval.

In this study, most of the subjects were elderly (aged over 65) with higher proportion of females suffered from ABU. The prevalence of ABU in the elderly has been estimated to be up to 35% for men and 50% for women in long term care facilities (Walker *et al.*, 2000). Higher infection rates in our elderly subjects are due to age-related alterations in immunity and other factors like diabetes and such a high prevalence of ABU in this study might be due to our diabetic subjects.

72.3% of cases with ABU suffered from diabetes and the prevalence of ABU in the diabetic elderly was significantly more than that for non-diabetic elderly subjects ($p < 0.05$). Similarly high incidence of a range of asymptomatic UTI in the diabetic elderly was reported in previous studies (Bonadio *et al.*, 2006). In Diabetes Mellitus altered leukocyte function contributes to the susceptibility to ABU in this disease (Balasoiu *et al.*, 1999).

Considering the higher number of females studied, the proportion of females affected by ABU in the present study was higher than the male cases in this study ($p < 0.05$). Other researches confirmed this too (Walker *et al.*, 2000; Tugrul *et al.*, 2005). The sexual dimorphism in the prevalence of ABU has been reported before in the healthy adults as well. Females are more prone to UTI and it is thought to be related to shorter urethra and the absence of antimicrobial substances of prostatic fluid, also a relative deficiency of secretory IgA antibody response from the mucosal surface in the urogenital tract of females as compared with males (Barza, 1993).

The infecting organisms identified in this study are similar to the commonly isolated bacteria in other studies. *E. coli* was the most common pathogen in this study (Fig. 1), as confirmed in other studies (Hooton *et al.*, 2000; Harding *et al.*, 2002; Yates, 1999; Rahav *et al.*, 2003). In another study the most prevalent bacteria isolated from

UTI in women and men were *E. coli* and *Proteus*, respectively (Orrett, 2001). In a study in Egypt on the ABU elderly subjects, the dominant bacterium was *klebsiellae* (El-Okle, Hamza and Abdel Aziz, 2004). It is interesting that the proportion of UTI caused by *E. coli* seems to be somehow different in various countries. We speculate that differences in temperature, climate, environment and/or antibiotic use may influence this. The presence of bacteria in the urine in the absence of symptoms suggests that there are alterations in the host pathogen interaction. For example it has been reported that uropathogenic strains of bacteria have evolved mechanisms to promote survival in the urinary space. The features of these adaptive mechanisms include presence of adhesion which promotes attachment to the urogenital tract and the production of factors such as α -haemolysin and cytotoxic necrotizing factor 1 or CNF1 (Stein and Funfstuck, 1999).

Antibiotic therapy for asymptomatic bacteriuria in institutionalized elderly people has not shown to be of benefit and may in fact be harmful (Walker *et al.*, 2000); however, in practice, antibiotics are still frequently used to treat asymptomatic bacteriuria in this population. Hundred percent resistance rate of isolated gram positives in this study to penicillin as a β -lactam antibiotic has commonly been reported in uropathogens from long-term care facilities (Nicolle, Strausbaugh and Garibaldi, 1996). Also, the increasing prevalence of extended spectrum β -lactamase producing organisms maybe the reason of such a (100%) resistance to cefazolin (Gales, 1997; Mamishi *et al.*, 2005) in our gram positive isolates. The finding of high resistance rate to tetracycline raises the assumption of whether these antibiotics are frequently prescribed inappropriately. This should be taken into consideration when formulating antibiotic policies in our country. Using broad-spectrum antibiotics has the disadvantage of promoting further resistance. Such a resistance data must play a correspondingly significant role when planning antibiotic policies. Vancomycin has also been widely used in Iran for the treatment of infection caused by methicillin-resistant staphylococci (Mamishi *et al.*, 2005). This might be the reason of high resistant rate (66.7%) to vancomycin our isolated Staphylococci.

More than half of all isolated bacteria in this study were resistant to co-trimoxazole. Resistance to co-trimoxazole has been frequently documented in nursing homes. Considering the high number of diabetic subjects (72.3%) in this study, an association has been found between the presence of *E. coli* co-trimoxazole resistance and diabetes, before (Wright *et al.*, 1999). Such a rate of resistance to co-trimoxazole we found in this study precludes, at least in our area, the choice of this or similar drugs in the empirical initial treatment of adult hospitalized patients with UTI.

The most isolated gram negative bacteria in our study were highly susceptible to aminoglycosides like amikacin (91.5%), gentamicin (87.8%) and tobramycin (82.1%). Similarly, in a study in Iran amikacin was shown to be very effective, with susceptibility rates of 84% in gram negative bacteria isolated from bloodstream infections (Mamishi *et al.*, 2005). However, up to 33% aminoglycoside resistance in gram-negative uropathogens has been reported before (Nicolle *et al.*, 1996).

Except for the only one resistant *Acenitobacter* isolate and the most (79%) of our *E. coli* isolates, 88.1% of other gram negatives and all of our Staphylococci isolates in this study were sensitive to ciprofloxacin as well. For the quinolones, in a survey in seven skilled nursing facilities in southern California, US, 12% of the isolates of the Enterobacteriaceae family and one-third of urinary *Pseudomonas* isolates were norfloxacin resistant approximately (Nicolle *et al.*, 1996), anyhow such a high resistance rate in the dominant uropathogenic *E. coli*, observed in this study reflect the possible indiscriminate application of ciprofloxacin in our area.

Antimicrobial agents are among the most frequent pharmaceutical agents prescribed in nursing homes. A high proportion of antimicrobial prescriptions given to nursing home patients are considered inappropriate and lead to antimicrobial resistance. No studies have defined the overall magnitude of this problem in a systematic manner. Present finding highlights the importance of a nationwide surveillance program to monitor the trends in isolation frequency of bacteria and their antimicrobial resistance patterns throughout Iran, as stated by other researchers (Mamishi *et al.*, 2005). However, prescribing antimicrobials for treatment of urinary infection is a part of the larger concern about difficulties in clinical diagnosis, appropriate antimicrobial use and the impacts of the selective pressure of antimicrobials on colonization and infection with resistant organisms in long-term care facilities.

In conclusion, the results of present study in Shiraz reconfirmed that unknown ABU is a significant problem in the residents of nursing homes especially older ones. It can be associated with symptomatic UTI caused by antibiotic resistance bacteria. Developing efficient institutional care and infection control along with surveillance program to control diabetes mellitus resulting in high rates of ABU in long term care facility residents especially in elderly subjects are strictly suggested.

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