

ORIGINAL ARTICLE

Asymptomatic bacteriuria prevalence and its relationship with urinary tract infections in the elderly

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ABSTRACT

Objective: The aim of this study was investigation of ASB prevalence and the relation for development of UTI in the people aged over 65 living in three nursing homes in Izmir province, Turkey.

Methods: The people aged over 65 in three nursing homes in Izmir, who did not suffer from any urinary system symptoms, on whom no urinary catheterizations were applied within the last 15 days, and who had not received any antibacterial treatments for the last one week for any reason, were included in the study between 2003 and 2004. First urine specimens were collected in the morning and the second were collected 24 to 48 hours later. ASB were included in clinical follow-up for six months and whether or not any UTI developed was recorded at intervals. At the third month, however, it was investigated whether ASB continued in patients or not. Patients were also examined in terms of ASB facilitating factors at same time.

Results: ASB was detected in 146 (24.1%) of 606 patients and more frequent in females than males (%27.8 vs. %18.6; p=0.009). The prevalence of ASB increased by age and length of stay in the nursing home. UTI was not developed and no death occurred in any of the patients during the follow-up period. At the third follow up month, it was observed that the ASB except *Proteus* spp. continued likewise.

Conclusion: The ASB prevalence was found as quite high in elderly in our country. Direct or indirect relationship between ASB and UTI has not been established. *J Microbiol Infect Dis* 2013; 3(1): 18-23

Key words: Asymptomatic bacteriuria, nursing homes, Urinary tract infections

Yaşlılarda asemptomatik bakteriüri prevalansı ve üriner sistem enfeksiyonları ile ilişkisi

ÖZET

Giriş: Ülkemizde 65 yaş üstü popülasyonda üriner sistem enfeksiyonu (ÜŞİ) gelişmesinde önemli yeri olan asemptomatik bakteriüri (ASB) prevalansı iyi tanımlanmamıştır. Bu çalışmanın amacı İzmir, Türkiye'deki 65 yaş üzeri huzurevi popülasyonunda ASB prevalansı ile üriner sistem enfeksiyonu gelişmesi arasındaki bağlantının araştırılmasıdır.

Metot: Bu çalışma İzmir'de üç büyük huzurevindeki 65 yaş üstü üriner sistem semptomu olmayan, son 15 gün içinde üriner kateterizasyon uygulanmamış ve herhangi bir nedenle son bir haftadır antibakteriyel tedavi almayanlar ve 2003 ile 2004 yılları arasında yapıldı. Hastalardan sabah ilk orta akım idrar örnekleri ve 24-48 saat sonra ikinci idrar örnekleri alındı. ASB tespit edilenler ve edilmeyenler altı ay klinik takibe alınarak aralıklarla üriner sistem enfeksiyonu gelişip gelişmediği kayıt edildi. Üçüncü ayda ise hastalarda ASB'nin devam edip etmediği araştırıldı. Hastalar aynı zamanda ASB'yi kolaylaştırıcı etkenler açısından da incelendi.

Bulgular: Toplam 606 hastadan 146'sında ASB tespit edildi (% 24,1). ASB sıklığı kadınlarda erkeklere göre daha sık idi (% 27,8 vs. % 18,6; p=0,009). ASB görülme oranının yaş ve huzurevindeki kalış süresiyle arttığı sonucuna varıldı. Takipte hastaların hiçbirisinde üriner sistem enfeksiyonu ve ölüm gelişmedi. Üçüncü aydaki kontrollerde *Proteus* spp. dışındaki ASB etkenlerinin aynen devam ettiği görüldü.

Sonuç: ASB prevalansı ülkemizde de yaşlılarda oldukça yüksektir. ASB ile üriner sistem enfeksiyonu arasında dolaylı veya doğrudan bir ilişki kurulamamıştır.

Anahtar kelimeler: Asemptomatik bakteriüri, huzurevi, üriner sistem enfeksiyonu

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INTRODUCTION

Urinary tract infection (UTI) is a diseases that observed frequently in children and the elderly (>65 yr). Especially the nursing home patients have the highest rate in this group. In these age groups, however, the presence of asymptomatic bacteriuria (ASB) can also be considered among the predisposing factors for UTI.¹⁻⁴ Besides all these, the fact that the bacteria causing UTI and ASB are identical has launched the question of whether ASB is a risk factor for UTI in geriatrics such as in pediatrics. Considering this situation, the discussion whether or not they are required to be treated.⁵

The term of ASB is defined by the growth of the same uropathogenic bacteria more than 10^5 cfu/ml in two different urine cultures, collected at 24-hour intervals from the patients without any symptoms and physical examination findings of UTI.^{1,2} The prevalence of ASB varies most frequently depending on age and gender. Particularly in childhood and in people aged over 65, prevalence is more frequent than the other age groups. Just like in UTI, the rate of ASB in females is higher than in males.^{3,4} The similar rates in both of these age groups can be attributed to the similarity of host factors.

There is no doubt that ASB is the colonization stage in the development of UTI. Because of increase of UTIs treatment costs in all age groups, recent discussions have concentrated on its prevention at the colonization stage. The question primarily awaiting answer at the focal point of these discussions is what the rate and speed of transformation of ASB into UTI are since the antimicrobial treatment to be provided will at the same time affect social health.

Although all similarities are known, there have not been any reliable studies that demonstrate the direct relationship yet.⁶⁻¹² Most of the studies conducted are studies including a short-term follow-up in few patient series. However, besides, there are also studies which followed for a long period of time like 14 years and concluded that it was not a risk factor for UTI.¹² Also in other studies, it has been demonstrated that yearly 0.11 to 0.15 of UTIs developed per bacteriuria particularly in patients with ASB in the nursing home and that 1 to 8% of them continued to be bacteraemic.^{13,14}

The prevalence of ASB, which is among the facilitative factors UTIs in over 65 age group, is not well defined in Turkey yet. The aim of this study was investigation of ASB prevalence and relation for development of UTI in the people aged over 65 living in the nursing homes in Izmir province, Turkey.

METHODS

Study design and patient selection

Three different nursing homes in Izmir (Narlidere, Gurcesme, and Yesilyurt districts) participated to this study between the years of 2003 and 2004. These nursing homes' guests were permanent and the population of per unit was between 168-424 elderly persons.

Patient selection criteria were as following

1. People aged >65 years,
2. People without any findings of lower and/or upper urinary system infections including dysuria, fever, and low back pain,
3. People without any applications of urinary catheter within the last two weeks,
4. People who were non-catheterized on the commencement of the study,
5. People in capable of providing midstream urine specimen by themselves,
6. People who had not received any antibiotic treatments for any reason within the last one week,
7. People who accepted being a part in the study.

Patient excluding criteria were as following

1. Not fulfilling any of the above mentioned criteria,
2. The people in whom mixed growth was found in the first urine specimen provided,
3. The people, who gave the first urine specimen but did not or unable to give the next urine specimen 24 to 48 hours later.

Sampling and microbiological studies

First morning voided urine specimens were collected using a midstream, clean-catch technique. Urine specimens were transported to the laboratory at the Dokuz Eylül University, Faculty of Medicine. Subjects were considered bacteriuric if a positive urine culture was confirmed by a second positive culture after 1-2 days from the first urine culture. All the urine specimens collected were cultured on plates within 30 to 45 minutes. Urine was plated by a loop quantification method on blood-based and MacConkey agars. Cultured plates were incubated under aerobic conditions at 37°C for 18 to 24 hours. Urinary specimens were considered positive if a single isolate in titres of 10^5 or more colony forming units (cfu) per milliliter of urine were obtained. The isolated microorganisms causing ASB were identified using standard microbiological methods. Antibiotic

susceptibility was determined by a disk diffusion test method (Kirby-Bauer). The isolates were also tested for the production of extended-spectrum beta-lactamase (ESBL) using the double-disk synergy screening test when *Escherichia coli* and *Klebsiella* spp. were identified.

Follow-up period of the patients

The patients diagnosed as ASB were followed in terms of the development of UTI. Each patient was observed every week where they stayed for a 6-month period, as part of routine medical care by the physicians of the unit. Antibiotics were not administered during the study period. All the patients were followed for six months in this way in terms of the development of UTI. The patients, which had similar risk factors but in which ASB was not found, were followed likewise. Each ASB diagnosed patient was sampled again at the third month of 6-month follow up period whether ASB continued or not. If it is continued we also investigated whether the same microorganism with previous ones or not.

Data collection and statistical analysis

From each patient the following demographic and microbiological data were collected: Age, gender, results of urine cultures, isolated microorganisms and results of antimicrobial susceptibility testing against antibiotics. Chi-square test was used for comparison of categorical variables. Tests were two-tailed, and *p* values of <0.05 were considered significant.

Statistical Package for the Social Sciences (SPSS) version 10.0 for Windows software was used for the statistical analysis and odds ratio (OR) and the 95% confidence interval (CI).

RESULTS

Patient characteristics and prevalence of ASB

A total of 937 elderly people in three nursing homes were included in the study. According to the distribution depending on nursing homes, 424 elderly people stayed in Narlidere Nursing Home affiliated to the Turkish Pension Fund whereas 168 elderly people stayed in Yesilyurt Nursing Home affiliated to the Ministry of Health and 345 in Gurcesme Nursing Home affiliated to Buca Municipality. Totally 690 out of 937 elderly people agreed to participate in the study. Since mixed bacterial growth was detected in the first urine specimen in 61 and the second urine specimen could not be collected in 23, 94 out of 690 patients were excluded from the study. Finally, a total of 606 patients (242 males and 364 females) were evaluated.

The mean age of the elderly people included in the study was 74.6±5.1 years while the mean of age of ASB patients was 76.6±3.4 years. The mean age was 73.5±3.3 years in males and 73.1±2.1 in females (*p* >0.05). However, in the ASB group, the mean age of females was 77.2±4.2 years and 72.1±2.9 years in males (*p*<0.001). ASB was detected in 101 (27.8%) out of 364 females and 45 (18.6%) out of 242 males (*p*=0.009).

Table 1. The distribution of asymptomatic bacteriuria (ASB) according to gender, age groups and length of stay (LOS) in nursing home centers (N=606).

| Variable | Present (N=146) | Absent (N=460) | Odds Ratio | 95% CI | P-value |
|--|-----------------|----------------|------------|------------|---------|
| Gender, n (%) | | | | | |
| Male (n=242) | 45 (18.6) | 197 (81.4) | 0.59 | 0.40-0.88 | 0.009 |
| Female (n=364) | 101 (27.8) | 263 (72.2) | | | |
| Age groups (yr), n (%) | | | | | |
| 65-69 (n=46) | 4 (8.7) | 42 (9.1) | 1.0 | | |
| 70-74 (n=330) | 50 (15.1) | 280 (60.9) | 1.87 | 0.68-6.37 | 0.247 |
| 75-79 (n=173) | 66 (38.1) | 107 (23.3) | 6.48 | 2.22-18.89 | <0.001 |
| 80 and above (n=57) | 26 (45.6) | 31 (6.7) | 8.81 | 2.78-27.82 | <0.001 |
| LOS in nursing home (yr), n (%) | | | | | |
| 0-2 (n=160) | 20 (12.5) | 140 (87.5) | 1.0 | | |
| 3-5 (n=247) | 74 (29.9) | 173 (70.1) | 2.99 | 1.74-5.14 | <0.001 |
| 6 and above (n=199) | 52 (26.1) | 147 (73.9) | 2.47 | 1.40-4.35 | 0.001 |

CI=Confidence interval; LOS=Length of stay

As it is shown in the table 1, the rate of ASB has increased with age. It is observed nearly eight times more in people aged over 80 than in the age group in 65-69. The fact that the highest increase takes place between the age group of 70-74 and the age group of 75-79 is observed between the second and third lines in the table. The difference between age groups was statistically significant ($p < 0.05$).

There was no significant difference in terms of length of stay (LOS) in nursing home for 3 to 5 years and staying for more than 6 years. Nevertheless,

when LOS in nursing home and prevalence of ASB were examined, it was observed that the actual significant difference was between staying for 0 to 2 years and staying for more than 2 years ($p < 0.05$; Table 1).

Microorganisms responsible for ASB (Table 2)

The most frequently isolated bacterium was *E. coli*, found in 59.6% of the positive urine cultures (87/146). *Klebsiella* spp. were found in 41 cultures (28.0%) and *Proteus* spp. were found in 18 cultures (12.4%).

Table 2. Distribution of microorganisms causing asymptomatic bacteriuria (ASB) according to nursing home centers.

| Microorganisms | Narlidere (N=63) | Gurcesme (N=48) | Yesilyurt (N=35) |
|-------------------------------------|------------------|-----------------|------------------|
| <i>Escherichia coli</i> (n=87) | 36 (57.3) | 27 (56.3) | 24 (68.6) |
| <i>Klebsiella pneumoniae</i> (n=23) | 9 (14.2) | 8 (16.6) | 6 (17.1) |
| <i>Klebsiella oxytoca</i> (n=18) | 7 (11.1) | 7 (14.6) | 4 (11.4) |
| <i>Proteus mirabilis</i> (n=15) | 9 (14.3) | 5 (10.4) | 1 (2.9) |
| <i>Proteus vulgaris</i> (n=3) | 2 (3.1) | 1 (2.1) | 0 (0.0) |

Antibiotic susceptibility of the isolates (Table 3)

Among the 146 isolates causing ASB, the most frequent resistance rates were observed against trimethoprim-sulfamethoxazole (TMP-SXT) and ampicillin. Nearly 80% of isolates were resistant against TMP-SXT and 71% of them were resistant against ampicillin respectively. Relatively low resistance rate (16.4%) was observed among them against ciprofloxacin, an antibiotic which is frequently prescribed in UTIs. No resistance to any of the studied third generation cephalosporins was detected and

no ESBL was found in any strains (data not shown). In addition, no amoxicillin-clavulanate and aztreonam resistance were detected accordingly (data not shown).

Except *Proteus* spp., ASB was discontinued in most patients. In 18 patients (128 / 146, 87.6%) ASB causing microorganisms (*P. mirabilis* and *P. vulgaris*) disappeared in the third month. During the six-month follow-up period, any of the patients with ASB developed lower and/or upper UTIs and no death was occurred.

Table 3. Antibiotic resistance ratio of the isolates causing asymptomatic bacteriuria (ASB) against some antibiotics

| Antibiotics | <i>E. coli</i> (n=87) | <i>K. pneumoniae</i> (n=23) | <i>K. oxytoca</i> (n=18) | <i>P. mirabilis</i> (n=15) | <i>P. vulgaris</i> (n=3) |
|----------------------|-----------------------|-----------------------------|--------------------------|----------------------------|--------------------------|
| Ampicillin, n (%) | 74 (85.0) | 20 (86.9) | 10 (55.5) | 0 (0) | 0 (0) |
| Ciprofloxacin, n (%) | 21 (24.1) | 3 (13.0) | 0 (0) | 0 (0) | 0 (0) |
| TMP-SMX, n (%) | 75 (86.2) | 21 (91.3) | 15 (83.3) | 5 (33.3) | 1 (33.3) |
| Norfloxacin, n (%) | 25 (28.7) | 3 (13.0) | 0 (0) | 0 (0) | 0 (0) |
| Amikacin, n (%) | 35 (40.2) | 19 (82.6) | 0 (0) | 0 (0) | 0 (0) |

TMP-SMX= Trimethoprim-sulfamethoxazole

DISCUSSION

The prevalence of ASB was found as 24% in this study. Like in other studies concerning ASB, the prevalence of ASB increased with age in our study.

When the age group of 65-69 and the age group of over 80 in the studied universe were compared, it was detected that ASB was observed nearly eight times more in this age group. In similar previous studies as well, the increase in the prevalence of

ASB with age has attracted the attention of many researchers. The physiological changes occurring with age particularly hormonal changes, the reduction in estrogen and the reduction in prostatic antibacterial factor facilitate colonization in the urethra, which is an entrance gate for bacteria. Especially besides hormonal changes, the lactobasillary reduction in vaginal flora is one of the important factors that facilitate the frequent prevalence of ASB in females in the alkali medium formed. The decreased turnover rate in the vaginal epithelium facilitates involvement for bacteria in atrophy and the dry medium formed. When the decrease in the number of defense cells and the simultaneous functional decrease among the physiological changes occurring with age combine with the decline in locally-effective sIgA level and the decrease in cytokine synthesis, the host defense factors also decrease.^{1-3,10,13,14}

When the relationship between gender and ASB was examined, it was observed that ASB was more frequent in female gender just like UTI. The fact that the distance between the bladder and “external urethral meatus” in females is anatomically shorter approximately by half than in males is known to be the most important factor.¹⁵

When it was examined whether the period spent in nursing home was effective in terms of ASB, a difference was found between staying for two years and staying for more than two years (Table 1). No statistically significant difference was found according to years. In similar studies, there are studies demonstrating that the prevalence of ASB increased as the period of stay in nursing home increased. It was showed previously that the rate of ASB increased approximately by 2 to 3 times among the residents of nursing home for 5 years and longer.¹⁴ Nevertheless, this increase seems to be related to age rather than the period spent. When the age groups of the same study are observed, it is seen that the people, who stayed in nursing home for more than 5 years, generally aged over 80 (93%) and that almost all of them were at the same time females.

In recurrent UTIs the damage in uroepithelium and submucosal tissue are together.^{1,14,15} Actually, when ASB is evaluated as the colonization stage prior to the development of UTI, this result is not surprising and it is an expected result. Naturally, since host-related facilitative factors cannot be prevented in the elderly, the frequently-suffered UTIs become outstanding as an increased risk factor for ASB.¹⁶⁻¹⁸

When we look at the bacterial agents causing ASB, they were found to be exactly the same with the studies in UTI and in literature.^{19,20} When they

were ordered from the most frequent to the least, they were found as *E. coli*, *K. pneumoniae*, *K. oxytoca*, *P. mirabilis* and *P. vulgaris*. When we look at their sensitivity pattern, TMP-SXT was striking as the antibacterial agent with the highest resistance rate among all bacteria. Recently, TMP-SXT resistance has been observed quite frequently among the agents of community-acquired UTI, particularly in data from the USA.²¹ TMP-SXT resistance was followed by ampicillin resistance in the antibiograms conducted. Although this study performed in the community, the other interesting result in this study is that ciprofloxacin resistance was found to be as 24% in all, particularly in *E. coli* isolates. However, no resistance was detected in the third generation cephalosporins tested among them. Moreover, no ESBL-positive strain was isolated in the study.

During the 6-month follow-up period, any lower and/or upper UTI developed and any ASB-dependent deaths were detected in the study. Thus, from our point of view, ASB does not constitute a sufficient indication alone in the elderly for antibacterial treatment.^{15,16}

The loss of *Proteus* spp. in the control urine cultures collected in the third month supports the hypothesis that ASB is a temporary colonization status. In any case, this ranks the first among the most important points that direct the recent discussions on the treatment concerning ASB. *Proteus* spp. are the bacteria with the lowest involvement capacity in uroepithelium among the uropathogenic bacteria. Thus, it is required that they should be the bacteria that naturally have to leave the stage the earliest in ASB, a picture identified as temporary colonization.^{6,8,22,23}

In conclusion, despite the presence of all facilitative factors, UTI did not develop in any of the patients during the six-month follow-up period and ASB-related mortality was found to be zero. Furthermore, it was detected that ASB continued likewise except for *Proteus* spp. in the urine cultures collected from the followed patients in the third month. The recent increase in TMP-SXT and ciprofloxacin resistance observed particularly in community-acquired *E. coli* strains was also verified here with the results.

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