

Urinary tract infection in a tertiary care hospital with special reference to Methicillin Resistant *S. aureus* (MRSA)

Ajantha GS, Kulkarni RD, Upadhya AK, Kalabhavi AS, Patil SS, Shetty PC, Shubhada RM, Jain PA

ABSTRACT

Background: Urinary tract infection (UTI) due to *S. aureus* is not uncommon, but published literature on its association with UTI is limited. It is well known for acquiring resistance to antibiotics. Therefore, it is essential to base the empirical therapy in reference to local susceptibility patterns. The aim of our study was to know the rate of *S. aureus* among all urinary isolates and to analyze their sensitivity patterns.

Materials and Methods: Urine samples received from suspected UTI cases over a period of one year were processed. All *S. aureus* isolates cultured from urine samples were included in the study. The antimicrobial susceptibility testing was performed by disk diffusion method and the resistance patterns of *S. aureus* were analyzed.

Results: Out of 1032 culture-proven UTI cases, *S. aureus* was the cause in 5.4% of cases. Majority (71.4 %) of *S. aureus* was isolated from urine samples of hospitalized patients and 66.1% were from females. Methicillin resistance was observed in 46.4% of the isolates. Multidrug resistance was noted in 73% of Methicillin resistant *S. aureus* (MRSA) isolates. Cotrimoxazole and fluoroquinolones were ineffective against majority of the isolates. Apart from vancomycin; Netilmicin and linezolid were also highly effective.

Conclusions: Considering the high isolation rate of MRSA and the associated multidrug resistance, therapeutic options remain very few. Regular updating of sensitivity pattern of the organism is important in amending the guidelines for therapeutic use of antibiotics based on evidence.

Keywords: MRSA, *Staphylococcus aureus*, urinary tract infection

INTRODUCTION

Urinary tract infection (UTI) is a common problem seen both in community as well as in hospital settings. It is one of those infections where antibiotics are frequently used. Empirical therapy is a rule rather than option in this condition, and a very few patients are treated according to culture and sensitivity test reports. The World Health Organization (WHO) has taken a serious note of antibiotic misuse and warned that we may head to the pre-antibiotic era if the attitude towards use of antibiotics is not drastically changed. As the slogan for World Health Day– 2011 indicates, we have to use antibiotics wisely, lest therapy in the future may become a tougher challenge.¹

UTI remains a major cause of morbidity especially in females.² The most common causative agent is

Escherichia coli in both community as well as hospital settings.^{3,4} Though *S. aureus* is less commonly encountered (2-15%), the isolation rate seems to be on the rise.^{5,6} Studies, especially addressing *S. aureus* in UTI are less frequently found in the published literature. Because of their potential to acquire resistance to multiple antibiotics (Multidrug resistance - MDR), therapeutic options are limited when staphylococcal UTI is encountered.^{7,8,9} Therefore, regular updating of therapeutic guidelines with reference to the sensitivity is essential. In the present study we intend to know the rates of *S. aureus* among all urinary isolates and to analyze their resistance patterns in our hospital with special importance to methicillin resistant *S. aureus* (MRSA).

MATERIAL AND METHODS

We studied all staphylococcal isolates from urine samples received in the laboratory at our hospital over a period of one year, from January 2010 to December 2010. All the urine samples were collected, transported and processed as per standard methods. The samples were inoculated on Blood agar and MacConkey agar. *S. aureus* isolates were identified by Gram stain, catalase test, coagulase test, mannitol fermentation and golden yellow pigment production.¹⁰

Antimicrobial susceptibility testing (AST) was performed by disc diffusion method as per CLSI guidelines.¹¹ The discs were either purchased from Himedia Laboratories, Mumbai or prepared in-house. Periodic quality assessment of the sensitivity discs and technique was performed using standard strains viz. *S. aureus* ATCC 25923, *E. Coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853. Cefoxitin discs were used to detect MRSA strains. The other antibiotics tested against *S. aureus* were penicillin (10 U), cotrimoxazole (1.25/23.75 µg), erythromycin (15 µg), clindamycin (2 µg), tetracycline (30 µg), gentamicin (10 µg), amikacin (30 µg), netilmicin (30 µg), norfloxacin (10 µg), ciprofloxacin (5 µg), ofloxacin (5 µg), linezolid (30 µg) and vancomycin (30 µg).

The data were analyzed considering the age, sex, hospitalization, methicillin resistance and the MDR characters. Strains resistant to three or more non-beta-lactam antimicrobial agents belonging to different classes were considered as MDR.¹²

RESULTS

Of the 1468 urine samples received for culture and sensitivity, 1032 were positive for bacterial cultures. Most common isolate was *E. coli*. We isolated 186 staphylococci from urine samples of which 56 were identified as *S. aureus*. Among the 56 samples positive for *S. aureus*, 40 were from hospitalized patients of which 13 (MSSA-6; MRSA-7) were catheterized. One patient had diabetic nephropathy and two cases had renal calculi. Methicillin resistance was noted in 26 isolates and the remaining 30 were MSSA (Table- 1). *S. aureus*

was isolated from 19 male patients and 37 females. Among the female patients, 17 were pregnant.

Table 1: *S. aureus* from UTI

Urinary isolates	Location		Total	Percentage
	Out Patient	In Patient		
MSSA	10	20	30	53.6
MRSA	06	20	26	46.4
Total <i>S. aureus</i>	16	40	56	100.0

Table 2: Resistance rates of *S. aureus* isolates

(N=56)		(N=30)	(N=26)
Antibiotic	Total <i>S. aureus</i> %	MSSA %	MRSA %
Contrimoxazole	53.6	30	80.8
Norfloxacin	37.5	16.7	61.5
Ciprofloxacin	44.6	30	61.5
Erythromycin	50.0	30	73.1
Clindamycin	23.2	6.7	42.3
Ofloxacin	26.0	00	50.0
Gentamicin	35.7	16.7	57.7
Netilmicin	00	00	00
Tetracycline	39.4	11.1	50.0
Linezolid	00	00	00
Vancomycin	00	00	00

Table 3: Multidrug resistant (MDR) isolates

Setting	MRSA	MSSA
OP	6	3
IP	13	2
Total	19	5

Most of the patients were adults belonging to the age group 18-65 years. In this study eight cases were found in above 65 years of age and four cases were below 18 years. All the six elderly male patients had ultrasonographically confirmed benign prostatic hypertrophy. The resistance rate of MRSA were considerably more compared to MSSA for the antibiotics tested (Table-2). An important observation was that all MSSA as well as all MRSA isolates were sensitive not only to vancomycin but also to linezolid and netilmicin. MDR strains were evidently more common in hospitalized patients and also with MRSA (Table -3).

DISCUSSION

The global occurrence of symptomatic UTI is estimated to be 150 million cases annually.¹³ The etiological agents have not changed their rank order significantly but their susceptibility patterns

to antimicrobials keep changing in an unfavorable manner. *E. coli* was the dominating bacterial species in the present study and *S. aureus* was the causative agent in 5.4% cases. The reported isolation rate of *S. aureus* in UTI is between 2% to 15%.^{4,5,14}

In the present study, 66 % of *S. aureus* isolates were from female patients and 71% of the isolates were from hospitalized patients. Both, female preponderance and increased risk with hospitalization are well established factors in UTI.^{2,14,15} Catheterization, another major risk factor for UTI, was noted in 32.5 % of hospitalized cases and MRSA was isolated from 53.9% of catheterized cases.

We noted that, 46.4% of *S. aureus* isolates were MRSA and most (73.1%) were MDR-MRSA. These infections are genuine therapeutic problems to the clinicians. The early initiation of therapy reduces the risk of progression from cystitis to pyelonephritis.¹⁶ Also, many of the staphylococcal bacteriuria may subsequently lead to bacteremia.¹⁷ Hence, clinicians often start the therapy empirically. However, selecting a drug for empirical therapy is difficult in these cases. Once we identify the isolate as MRSA all beta-lactam antibiotics are excluded from therapeutic options. MDR-MRSA being resistant to many other antibiotics there is further narrowing down of the treatment options. It especially poses the greatest challenge while treating pregnant women from this group.¹⁸ In our study, 36.8 % of MDR-MRSA isolates were from this important group (7 out of 19).

Since *S. aureus* is known for multidrug resistance, knowledge of local susceptibility pattern is important. In the present study, highest resistance rates (> 80%) were noted against co-trimoxazole which is one of the empirical drugs of choice in uncomplicated UTI.² Similarly, higher resistance rates were seen against common anti-staphylococcal agents like erythromycin and ciprofloxacin with 50% and 44.6% strains being resistant respectively. Norfloxacin, one of the commonly used empirical antibiotics for UTI, was

not found to be very active against *S. aureus* (37.5% resistant). Among the tested aminoglycosides, netilmicin was effective against 100% of the isolates tested in vitro whereas more than 35% of the isolates were resistant to gentamicin. Netilmicin, like any other aminoglycoside, is a parenteral drug and is not the safest choice in pregnant ladies and in elderly.^{18,19} In hospitalized male patients as well as non-pregnant females with normal renal functions, this drug can be an important alternative antibiotic whenever the organism is not susceptible to other less toxic antimicrobials. It has been noted to be a very useful prophylactic agent for preventing UTI in genitourinary surgery.²⁰ All the isolates were also sensitive to vancomycin and linezolid. Both these drugs are expensive and vancomycin is a reserve drug for serious infections only.²¹ Linezolid has the added advantage of being available in oral formulation. Though it is very effective against the strains isolated from urine in vitro, published data on its usage in UTI is scarce.^{21,22,23}

We did not test another important therapeutic choice i.e., nitrofurantoin. Of late, we have included this drug for testing panel and it was active against all *S. aureus* isolates from urine samples including MRSA. This seems to be a very effective drug in our set up. However, the number of isolates tested is still very small (MRSA – 9 isolates) to draw conclusions. Among the newer agents, daptomycin is a promisingly effective agent for UTI and tigecycline needs further evaluation for the usage in UTI.²¹ However, we have not tested our isolates against these drugs.

Rapid detection of a staphylococcal isolate as MRSA may help in timely initiation of an appropriate therapy based on the local susceptibility data. This, in fact, may reduce the unnecessary usage of ineffective antibiotics. The detection of MECA by molecular methods or PBP2A by latex agglutination test can be helpful for this purpose, provided they become more affordable to the patients.²⁴

CONCLUSION

UTI due to *S. aureus* is a therapeutic problem.

MDR-MRSA leaves very few choices for treating UTI caused by them. Appropriate therapy should be based on the local antibiotic sensitivity pattern for which periodic review of the susceptibility data is essential. Drug resistance is a huge concern today and therefore, awareness about the rationale of judicious antibiotic use cannot be overemphasized

AUTHOR NOTE

Ajantha GS, Associate Professor, Contact- +91836-2477374, 2477256,

E-mail: ajju_dwd@rediffmail.com

(Corresponding Author)

Raghavendra D. Kulkarni, Professor & Head

Amruth Kishen Upadhyaya, Assistant Professor

Anuradha S. Kalabhavi, Assistant Professor

Satish S. Patil, Assistant Professor

Praveen C. Shetty, Assistant Professor

R. M. Shubhada, Lecturer

Jain Amrath Pavithra, Tutor

Department of Microbiology, SDM College of Medical Sciences & Hospital, Sattur, Dharwad – 580009, India.

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