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Research Article

URINARY TRACT INFECTION BY COAGULASE NEGATIVE STAPHYLOCOCCI AND STAPHYLOCOCCUS AUREUS WITH SPECIAL REFERENCE TO MRSA

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A R T I C L E I N F O

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A B S T R A C T

Background: Urinary tract infection (UTI) is a frequent cause of morbidity both in the community and in the hospital setting. It is one of those infections where empirical antibiotics are frequently used. *S. aureus* is an opportunistic pathogen affecting both immune competent and immunocompromised individuals. Methicillin-resistant *S. aureus* (MRSA) is widespread and is increasingly seen in community health care units. MRSA infections occur most frequently among persons in hospitals and healthcare facilities such as nursing homes and dialysis centers, who have weakened immune systems. MRSA strains with decreased susceptibility to vancomycinand strains fully resistant to vancomycin (MIC ≥ 16 µg/ml) have been reported.

Materials and Methods: The study was performed from January 2017 to December 2017. Urine samples collected in appropriate sterile manner were screened for pus cells and bacteria by routine microscopic examination. This was followed by plating on MacConkey's agar and Blood agar. Inoculated plates were incubated overnight at 37 ^{0}C. Isolated catalase positive Staphylococcus species were identified with Matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) to confirm the speciation. Antibiotic susceptibility was performed by Vitek compact 2 as per CLSI guidelines establishing MIC (Minimum Inhibitory Concentration).

Results: Of the 158 isolates of *S. aureus*, 41 (25.94%) were MRSA. Of the 58 isolates *of S. saprophyticus*, 23 (39.65%) were methicillin resistant (MRCONS). Cefoxitin was used as a surrogate marker for methicillin and oxacillin resistance.Of the 158 isolates of *S. aureus*, 4 strains were resistant to vancomycin (VRSA) with MIC values more than 32 µg/ml and one strain was intermediate with MIC of 4 µg/ml. Of the 58 isolates of *S. saprophyticus*, one strain was resistant to vancomycin with MIC 32 µg/ml. The isolates of *Staphylococcus aureus* which were intermediate to vancomycin (VISA) and resistant to vancomycin (VRSA) were re-tested with vancomycin E (Biomerieux-Etest strips) to compare the results with automated susceptibility testing.

Discussion: The worldwide incidence of symptomatic urinary tract infection is estimated to be around 150 million cases annually. Urinary catheterization is one of the major risk factor for development of UTI in hospitalized patients. A UTI in the presence of a urinary catheter warrants removal or changing of the catheter. Most of the MRSA isolates (N=41) in our study were from catheterized patients. Since *S. aureus* is known for multidrug resistance, knowledge of local antimicrobial susceptibility pattern is important in an order to choose empirical therapy. In the present study, we have noted highest drug resistance rates among Fluoroquinolones with ciprofloxacin (87.34%) and levofloxacin (70.88%) which are one of the empirical drugs in treatment of uncomplicated UTI.

Conclusion: MRSA is one of the most prevalent nosocomial pathogens worldwide. MRSA strains which are multidrug resistant (MDR) leaves very few options for treating UTI. Appropriate therapy should be based on the local antimicrobial susceptibility pattern for which periodic review of the antibiogram is essential. Rapid detection of a staphylococcal isolate especially MRSA may help in timely initiation of an appropriate therapy. Drug resistance is a huge concern today and therefore, awareness about the rationale of judicious antibiotic use cannot be overemphasized.

INTRODUCTION

Urinary tract infection (UTI) is a frequent cause of morbidityboth in the community and in the hospital setting[1, 2]. 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.

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The causative pathogen can vary greatly geographically, and so it is prudent to identify those with resistant strains and have current data on the appropriate empirical therapy within a region. The most frequently encountered organisms associated with UTIs include enteric Gram-negative bacteria (with Escherichia coli being the most predominant), coagulase negative Staphylococci like *S.saprophyticus* along with Proteus and Klebsiella species, Enterococcus, and *S. aureus* which account for less than 5%[3]. However, recent studies have reported the increasing prevalence of *Staphylococcus aureus* in UTIs[4, 5, 6]. *S. aureus* is an opportunistic pathogen affecting both immune competent and immunocompromised individuals,

frequently resulting in significant morbidity. Many strains of *S. aureus* carry a wide variety of multidrug-resistant genes on plasmids, which aid the spread of resistance among species[7]. Methicillin-resistant *S. aureus* (MRSA) is widespread and is increasingly seen in community health care units[8]. MRSA infections occur most frequently among persons in hospitals and healthcare facilities such as nursing homes and dialysis centers, who have weakened immune systems. However, these infections are occurring increasingly in the community. Currently there are two genetically different strains of MRSA circulating in the United States. One is called Community-acquired MRSA (CA-MRSA) and the other is Healthcare-associated MRSA (HA-MRSA). CA-MRSA isolates usually are resistant only to ß-lactam agents and erythromycin and can be treated with a variety of other antibiotics. Since 1996, MRSA strains with decreased susceptibility to vancomycin (minimum inhibitory concentration (MIC> 4-8 µg/ml) and strains fully resistant to vancomycin (MIC ≥ 16 µg/ml) have been reported[9]. Globally, it is considered that there has been an epidemic of MRSA within health care institutions[10, 11]. Bacteriuria with *S. sureus* is hypothesized to occur through a number of mechanisms that includes catheterization, urologic procedures, or seeding of the genitourinary tractincluding nephrologically excreted bacteria in overt bacteremia. Bacteremia itself is associated with bacteriuria in patients infected with *S. sureus*, which suggests that bacteremia is an important precursor for bacteriuria in some patient groups[12, 13]. However, little is published on the features of MRSA-positive urine cultures. Herein, we chronologically assessed the source, patient demographics, and antimicrobial susceptibilities of MRSA-positive isolates. In the present study we intend to know the rates of *S.aureus* and other coagulase negative staphylococciamong urinary tract isolates and to analyze their resistance patterns with special importance to methicillin resistant *S.aureus* (MRSA).

MATERIALS AND METHODS

All the urine (midstream, catheter) specimens collected from patients with suspected UTI were cultured on blood agar and MacConkey's agar in the Department of Microbiology, Metropolis healthcare limited, Mumbai, India. During the study period (January 2017 to December 2017), Gram-positive, catalase positive cocci, beta haemolytic or non-haemolytic colonies isolated in significant counts ($>1\times10^5$cfu/ml) in pure culture were included in the study. The records of the patients whose urine samples grew methicillin resistant *S. aureus* (MRSA) with MIC values more than 8 µg/ml in significant numbers were retrospectively reviewed for demography, clinical findings, underlying medical problems, surgical procedures, invasive devices, and treatment with antimicrobial agents and outcome.Cefoxitin is used as a surrogate marker for oxacillin or methicillin resistance to detect MRSA. Methicillin or oxacillin is reported as susceptible or resistant based on cefoxitin results. UTI was defined as the presence of any one of the following symptoms: fever, burning, urgency, frequency of micturition, supra pubic tenderness and growth of 10^5cfu/ml of Staphylococcus species from urine specimen. Some researchers may consider colony count of 1×10^2 CFU/ml for *S. aureus* to be significant count in the urine with symptoms suggestive of UTI. Patients with suprapubic aspiration, growth of even single colony of *S. aureus* is considered significant. The objective of this study was to determine the antibiotic susceptibility pattern of the isolated strains Staphylococci with special reference to MRSA and to guide clinicians for appropriate treatment for reduction of morbidity & mortality. This study was performed with patients admitted in a tertiary care hospital, developing symptoms of UTI at least after 48 hours of admission. Some patients from community acquired infection with symptoms of UTI have also been included in the study. Cases of urinary tract infection with established nonbacterial etiology (fungal UTI) excluded from the study. The study was performed over a period of one from January 2017 to December 2017. Urine samples collected in appropriate sterile precautions were screened for pus cells and bacteria by routine microscopic examination. This was followed by plating on MacConkey's agar media (differential & partially selective media), Blood agar (enriched media producing white, opaque hemolytic or non-hemolytic colonies in sheep blood agar). Inoculated plates were incubated overnight at 37^0c. Isolated Staphylococcus strains were identified with Matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) to confirm the speciation. Antibiotic susceptibility was performed by Vitek compact 2 (Biomerieux France) as per CLSI guidelines establishing MIC (Minimum Inhibitory Concentration) of the tested antibiotics. The isolates of *Staphylococcus aureus* which were intermediate to vancomycin (VISA) and resistant to vancomycin (VRSA) were re-tested with vancomycin E (Biomerieux-Etest strips) to compare the results with automated susceptibility testing.

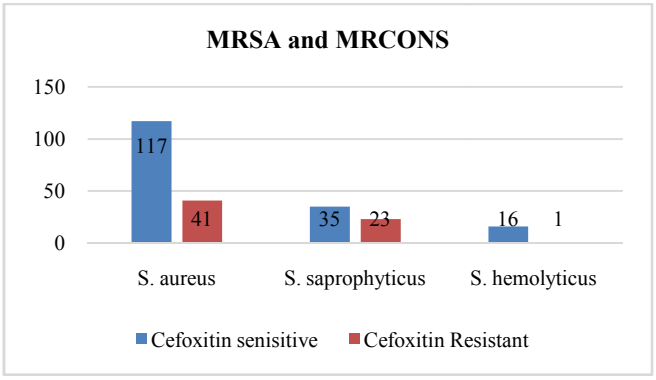
RESULTS

Table 1 Minimum inhibitory concentrations (MIC) of antimicrobials used for Staphylococcus species causing urinary tract infections adapted from CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 27th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.S= Susceptible; I= Intermediate; R= Resistant.

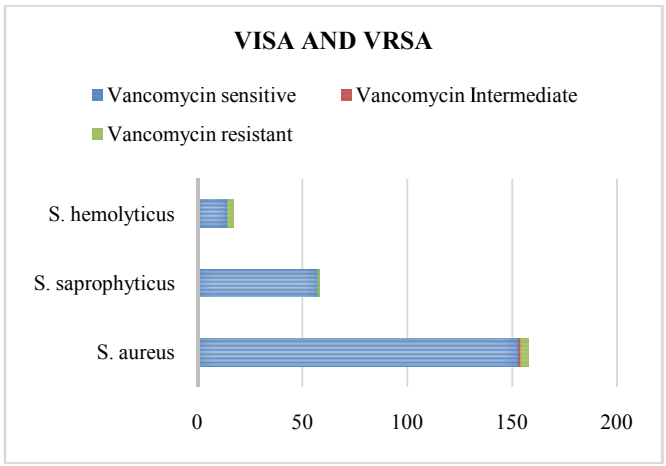
Antibiotic	MIC			Comments
	S	I	R	
Cefoxitin	<=4	-	>=8	Cefoxitin is tested as a surrogate for oxacillin; report oxacillin susceptible or resistant based on the cefoxitin result.
Vancomycin	<=2	4-8	>=16	MIC tests should be performed to determine the susceptibility of all isolates of staphylococci to vancomycin.
Teicoplanin	<=8	16	>=32	-
Linezolid	<=4	-	>=8	When testing linezolid, disk diffusion zones should be examined using transmitted light. Organisms with resistant results by disk diffusion should be confirmed using an MIC method.
Erythromycin	<=0.5	1-4	>=8	Inducible clindamycin resistance can be detected by disk diffusion using the D-zone test or by broth microdilution
Clindamycin	<=0.5	1-2	>=4	
Daptomycin	<=2	-	-	Daptomycin should not be reported for isolates from the respiratory tract.
Nitrofurantoin	<=32	64	>=128	
Ciprofloxacin	<=1	2	>=4	-
Levofloxacin	<=1	2	>=4	
Penicillin	<=0.12	-	>=0.25	Penicillin should be used to test the susceptibility of all staphylococci to all penicillinaselabile penicillins. For oxacillin-resistant staphylococci report penicillin as resistant or do not report.
Rifampin	<=1	2	>=4	Rifampin should not be used alone for antimicrobial therapy.
Cotrimoxazole	<=2/38	-	>=4/76	
Tetracycline	<=4	8	>=16	-
Gentamicin	<=4	8	>=16	

Table 2 Susceptibility pattern of different species of Staphylococci from urinary tract isolates.
S= Susceptible; I= Intermediate; R= Resistant;ICR[#]- Inducible Clindamycin Resistance
Daptomycin* has been tested for 53 isolates of *S. aureus,* 11 isolates of *S. saprophyticus*

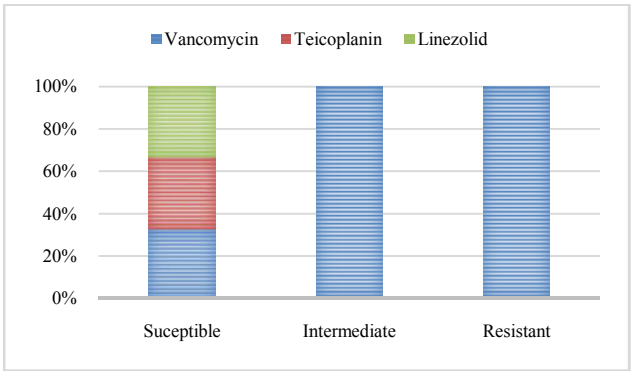
Organism (N=238) /	Staphylococcus aureus (N=158)			Staphylococcus saprophyticus(N=58)			Staphylococcus epidermidis(N=05)			Staphylococcus hemolyticus(N=17)		
Drugs	S	I	R	S	I	R	S	I	R	S	I	R
Oxacillin/Cefoxitin	117	-	41	35	-	23	4	-	1	1	-	16
Vancomycin	153	1	4	57	0	1	5	0	0	14	-	3
Teicoplanin	158	0	0	58	0	0	5	0	0	16	1	0
Linezolid	158	0	0	58	0	0	5	0	0	17	0	0
Erythromycin	93	13	52	27	2	29	3	1	1	1	0	16
Clindamycin	116	11	31	30	0	28	4	0	1	2	0	15
ICR[#]	132	-	26	55	-	3	4	-	1	10	-	7
Daptomycin*	53	-	-	11	-	-	-	-	-	-	-	-
Nitrofurantoin	147	3	8	56	0	2	5	0	0	16	0	1
Ciprofloxacin	18	2	138	51	0	7	3	0	2	1	1	15
Levofloxacin	19	27	112	51	0	7	4	0	1	2	1	14
Penicillin	103	-	55	0	0	58	0	0	5	17	0	0
Rifampin	148	3	7	56	0	2	5	0	0	15	0	2
Cotrimoxazole	98	-	60	50	0	8	1	0	4	11	0	6
Tetracycline	113	9	36	54	0	4	2	0	3	5	0	12
Gentamicin	131	2	25	55	0	3	4	0	1	8	4	5



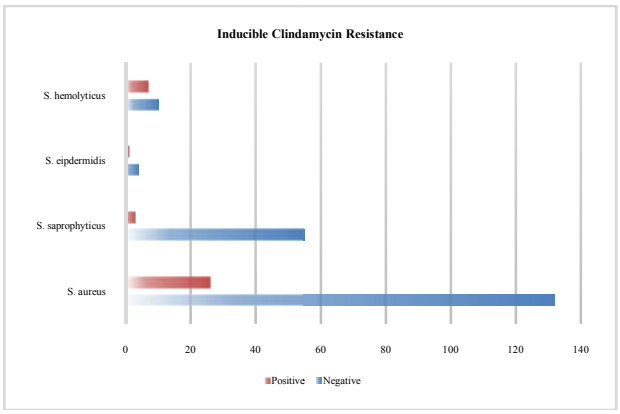
Graph 1 Of the 158 isolates of *S. aureus*, 41 (25.94%) were MRSA. Of the 58 isolates *of S. saprophyticus*, 23 (39.65%) were methicillin resistant. Cefoxitin is used as a surrogate marker for methicillin and oxacillin testing.



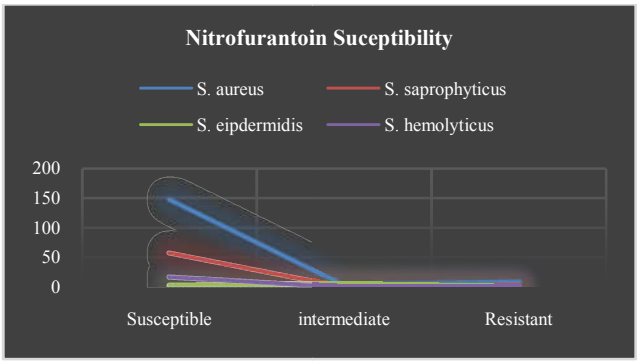
Graph 2 Of the 158 isolates of *S. aureus*, 4 strains were resistant to vancomycin (VRSA) with MIC values more than 32 µg/ml and one strain was intermediate with MIC of 4 µg/ml. Of the 58 isolates of *S. saprophyticus*, one strain was resistant to vancomycin with MIC 32 µg/ml.



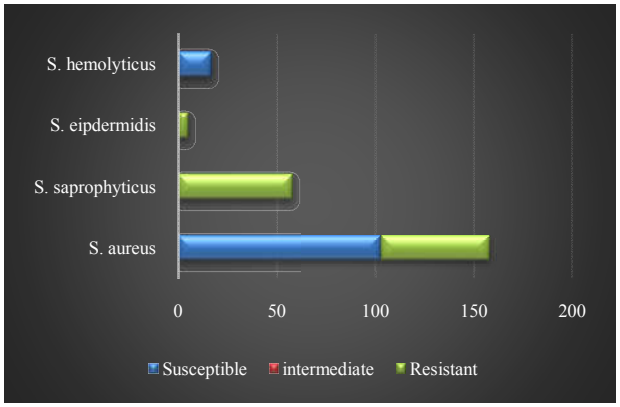
Graph 3 Susceptibility of *S. aureus* with vancomycin, teicoplanin and linezolid. None of the isolates of *S. aureus* shown resistance to teicoplanin and linezolid.



Graph 4 Inducible clindamycin resistance in different species of Staphylococci. Of the 158 isolates of *S. aureus,* 26 (16.45%) were ICR positive and 132 were negative.



Graph 5 Susceptibility of nitrofurantoin with Staphylococcus species. Nitrofurantoin which achieves good urinary concentration is a good option for treatment of UTI.



Graph 6 Penicillin susceptibility with Staphylococcus isolates. All the 58 isolates of *S. saprophyticus*and 5 strains of *S. epidermidis* were resistant to Penicillin. Penicillin should be used to test the susceptibility of all staphylococci to all penicillinase labile penicillins. For oxacillin-resistant staphylococci, penicillin is reported as resistant.

DISCUSSION

The worldwide incidence of symptomatic urinary tract infection is estimated to be around 150 million cases annually[14]. The etiological agents have not changed their rank order significantly but their susceptibility patternsto antimicrobials keep changing in an unfavorable manner. *E. coli* and other Gram negative bacilli belonging to *Enterobacteriaceae* family and Gram negative non fermenters like *P. aeruginosa* and *Acinetobacter* species were the dominant isolates from urinary tract in the present study but*S. Aureus* was the causative agent in 3.9% of total culture positive cases. The reported isolation rate of *S. aureus* in UTI is between 2% to 15%[15, 16, 17]. In the present study, 97 (61.39 %) of *S. aureus* isolates were from female patients and 61 (38.60%) of the isolates were from male patients. Of the 58 isolates of *S. saprophyticus*, 51 were from female and 7 isolates were from male patients. Both, female preponderance and increased risk with hospitalization and pregnancyare well established factors in UTI[18, 19]. Urinary catheterization is one of the major risk factor for development of UTI in hospitalized patients. Urinary catheters are likely to lead to colonization of the bladder and subsequent infection. Bacteria adhere to the catheter surface and contribute to the production of a biofilm composed of bacteria, bacterial glycocalyces, host proteins, and urinary salts like apatite and struvite. The bacteria travel beneath this biofilm along the catheter into the bladder. Brief use of indwelling urinary catheters after operations or in critically ill patients to measure urine output will not result in infection for up to 7 days if the catheter connections are left undisturbed and a closed drainage system is scrupulously maintained. Long-term use of urinary catheters will always result in colonization and infection. A UTI in the presence of a urinary catheter warrants removal or changing of the catheter. Most of the MRSA isolates (N=41) in our study were from catheterized patients. We observed that, of the 158 isolates of *S. aureus*, 41 (25.94%) were MRSA. Of the 58 isolates *of S. saprophyticus*, 23 (39.65%) were methicillin resistant (MRCONS). These infections are genuine therapeutic problems to the clinicians. The early initiation of antimicrobial therapy reduces the risk of progression from cystitis to pyelonephritis in critically ill patients[20]. Methicillin-resistant *S. aureus* strains have acquired resistance to methicillin and other beta lactam antibiotics (e.g., penicillins and cephalosporins) via the mecA or mecC genes. Most MRSA carry the mecA gene, which resides on a large mobile genetic element called the staphylococcal chromosomal cassette mec (SCCmec). This gene codes for a penicillin binding protein, PBP2a, which interferes with the effects of beta lactam antibiotics on cell walls. It confers virtually complete resistance to nearly all beta-lactam antibiotics including semi-synthetic penicillins such as methicillin, oxacillin, or cloxacillin. Exceptions to this rule are the latest generation of cephalosporin β-lactams, e.g., ceftaroline and ceftobiprole which have anti-MRSA activity. Acquisition of mecA seems to have occurred independently in a number of *S. aureus* lineages. Some lineages have a tendency to colonize specific species, and may be adapted to either humans or animals. MRSA strains known as epidemic strains are more prevalent and tend to spread within or between hospitals and countries. Other "sporadic" strains are isolated less frequently and do not usually spread widely. There are also MRSA strains that produce various exotoxins (e.g., toxic shock syndrome toxin 1, exfoliative toxins A or B, and enterotoxins) associated with specific syndromes, such as toxic shock syndrome. MecC (formerly mecALGA251) is a beta lactam resistance gene that was first recognized in 2011, and is less well understood than mecA. Like mecA, mecC is carried on SCCmec. It codes for a different version of PBP2a, which is also thought to interfere with the effects of beta-lactam antibiotics on cell walls. However, a recent paper suggests that mecC-encoded PBP2a may mediate resistance to some. Cefoxitin is used as a surrogate marker for *mecA*-mediated oxacillin resistance. Isolates that test as *mecA* positive should be reported as oxacillin (not cefoxitin) resistant; routine testing of other β lactam agents, except those with anti-MRSA activity, is not advised. Because of the rare occurrence of oxacillin resistance mechanisms other than *mecA,* isolates that test as *mecA* negative, but for which the oxacillin MICs are resistant (MIC >=4 µg/mL), should be reported as oxacillin resistant. Many of the staphylococcal bacteriuria may subsequently lead to transient to frank bacteremia and urinary sepsis[21]. Therefore, clinicians often start the therapy empirically antimicrobials. Selecting a drug for empirical therapy is difficult in these cases. Once we identify the isolate as MRSA all beta-lactamantibiotics 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[22]. Since *S. aureus* is known for multidrug resistance, knowledge of local antimicrobial susceptibility pattern is important in an order to choose empirical therapy. In the present study, we have noted highest drug resistance rates among Fluoroquinolones with ciprofloxacin (87.34%) and levofloxacin (70.88%) which are one of the empirical drugs of choice in uncomplicated UTI. Similarly, higher resistance rates were seen against common anti-staphylococcal agents like erythromycin, penicillin and cotrimoxazole. Nitrofurantion, one of the commonly used empirical antibiotics for UTI, was found to be very active against *S. aureus* as it achieves a very good urinary concentration. Of the 158 isolates of *S. aureus*, 147 were sensitive and 8 were resistant to nitrofurantoin. We have tested aminoglycosides like Gentamicin, of which 82% of S. aureus were susceptible. Netilmicin, like any other aminoglycoside, is a parentral drug and is not the safest choice in pregnant ladies and in elderly[23]. 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[24]. Of the 158 isolates of *S. aureus*, 4 strains were resistant to vancomycin (VRSA) with MIC values more than 32 µg/ml and one strain was intermediate with MIC of 4 µg/ml. Of the 58 isolates of *S. saprophyticus*, one strain was resistant to vancomycin with MIC 32 µg/ml.The isolates of *Staphylococcus aureus* which were intermediate to vancomycin (VISA) and resistant to vancomycin (VRSA) were re-tested with vancomycin E (Biomerieux-Etest strips) to compare the results with automated susceptibility testing. The Etest results have shown concordance with automated susceptibility testing. All the isolates were also susceptible to teicoplanin and linezolid. Both these drugs are expensive and vancomycin and teicoplaninare reserve drugs for serious infections only[25]. 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[26, 27]. The newer agents like, daptomycin is a promisingly an effective agent for UTI. We have tested for 53 isolates of *S. aureus* and 11 isolates of *S. saprophyticus*. All the strains were found susceptible to daptomycin with lower MIC. Note that as per CLSI, daptomycin should not be reported from isolates of respiratort tract. We have not tested any isolate for tigecycline susceptibility. As per recommendations it needs to be used in bone and soft tissue infections, gastrointestinal and blood stream infections. The role tigecycline in UTI needs further evaluation. Of the 158 isolates of S. aureus, 103 (65.18%) were susceptible and 55 (34.81%) were resistant. All the 58 isolates of *S. saprophyticus* and 5 strains of *S. epidermidis* were resistant to Penicillin indicating the higher prevalance of coagulase negative staphylococcic producing β lactamase. Penicillin should be used to test the susceptibility of all staphylococci to all penicillinase labile penicillins. For oxacillin-resistant staphylococci, penicillin is reported as resistant. The penicillin disk diffusion zone-edge test was shown to be more sensitive than nitrocefin based tests for detection of β lactamase production in *S. aureus*. The penicillin zone-edge test is recommended if only one test is used for β lactamase detection. However, some laboratories may choose to perform anitrocefin-based test first and, if this test is positive, report the results as positive for β lactamase (or penicillin resistant). If the nitrocefin test is negative, the penicillin zone-edge test should be performed before reporting the isolate as penicillin susceptible in cases where penicillin may be used for therapy (eg,endocarditis) [28, 29].

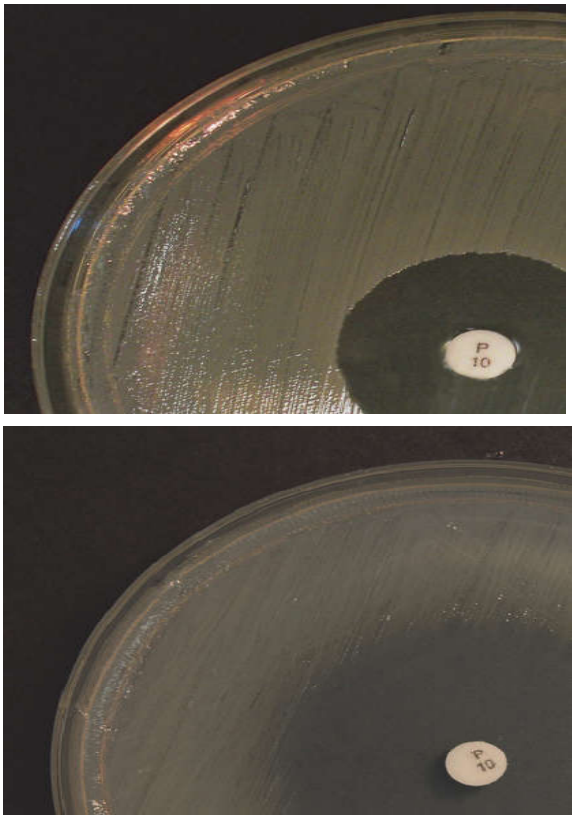


Figure 1 A Positive Penicillin Disk Zone-Edge Test for β-Lactamase Detection. The zone edge is sharp or like a "cliff" indicating β lactamase production. A Negative Penicillin Disk Zone-Edge Test for β-Lactamase Detection. The zone edge is fuzzy or like a "beach" indicating no β lactamase production.Adapted from CLSI; Performance Standards for Antimicrobial Susceptibility Testing. 27th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.

For *S. lugdunensis,* tests for β lactamase detection are not necessary because isolates producing a β lactamase will test penicillin resistant (MIC > 0.12 µg/mL and zone diameters < 29 mm). If a laboratory is using a method other than the CLSI disk diffusion or MIC reference method and is unsure if the method can reliably detect penicillin resistance with contemporary isolates of *S. lugdunensis,* the laboratory should perform an induced nitrocefin assay or other CLSI reference method on isolates that test penicillin susceptible before reporting the isolate as penicillin susceptible.Of the 158 isolates of *S. aureus* 26 (16.45%) were positive for ICR (inducible clindamycin resistance) and 132 were negative. Flattening of the zone of inhibition adjacent to the erythromycin disk (referred to as a D-zone) indicates inducible clindamycin resistance. Hazy growth within the zone of inhibition around clindamycin indicates clindamycin resistance, even if no D-zone is apparent. Isolates with inducible clindamycin resistance are reported as clindamycin resistant. In routine clinical practice clindamycin is not used to treat UTI as it is highly nephrotoxic and is to be reserved for treatment of anaerobic infections. *S. saprophyticus* is the second most frequent cause of uncomplicated UTI in women after *E. coli*. Majority of infections occur in young sexually active women. Significantly more patients infected with *S. saprophyticus* complain of dysuria, urinary frequency, and back pain than do patients infected with *E. coli*[30, 31]. It is referred to as "honeymooner's" UTI causing cystitis due to its association with sexual intercourse. There are also several case reports of infections in young girls[32]. The more severe complications include cystitis, acute pyelonephritis, septicemia, nephrolithiasis and endocarditis[33, 34, 35]. *S. saprophyticus* can also cause UTI in males of all ages. The organism has been isolated in young boys, male homosexuals, and elderly men with indwelling urinary catheters[36, 37]. It also can cause urethritis, epididymitis, prostatitis, and nephrolithiasis in men, and is relatively rare in hospitalized men[38]. *S. saprophyticus* is usually susceptible to antibiotics commonly prescribed for patients with UTI, with the exception of nalidixic acid. Furthermore, in women with acute uncomplicated cystitis, empirical therapy without a urine culture is often used. The rationale for this approach is based on the highly predictable spectrum of etiologic agents causing UTI and their antimicrobial resistance patterns. However, antimicrobial resistance among uropathogen causing community-acquired UTIs, both cystitis and pyelonephritis, is increasing[39]. The present studyalso emphasizes the rate of isolation of *S. saprophyticus* as a cause of UTI among different age and sex and their resistant pattern against commonly used antibiotics. In our study, *S. saprophyticus* was susceptible to cotrimoxazole, tetracycline and nitrofurantoin. Combination of sulfamethoxazole and trimethoprim was once the first-line antibiotic for use in *Staphylococcus* UTIs as it is inexpensive, is effective against *S. saprophyticus* and is excreted in active form in urine. Nitrofuratoin is another drug that achieves good concentration in bladder, is a safe option for treatment of UTI by *S. saprophyticus* especially in pregnant women. Fluoroquinolones are preferred as initial agents for empiric therapy of UTI. Of the 58 isolates of *S. saprophyticus* 51 isolates were susceptible to both ciprofloxacin and levofloxacin. However development of resistance to fluoroquinilones is a major concern in recent years[40, 41]. So, isolation & identification of urinary pathogens with their sensitivity pattern should be done routinely. *S. epidermidis* and

S. hemolyticus commonly causes infections associated within dwelling central venous catheters, cerebrospinal fluids hunts, prosthetic heart valves, and peritoneal dialysis catheters. When these organisms are isolated from blood or body fluids in patients without predisposing factors, it is often considered a contaminant. Urinary tract infections caused by *S.epidermidis* and *S. hemolyticus* are often associated with instrumentation of the urinary tract in a hospital setting, including neonates in the neonatal intensive care unit. The potential pathogenicity of these coagulase negative staphylococci (CONS) in causing urinary tract infection is not known. These isolates are included in the study because most of these patients have undergone urinary catheterization and showed significant colony count with presence of polymorphonuclear leucocytes (PMNL) in the urine. Also the fact that CONS found to be more resistant to commonly used antimicrobials for treatment of UTI as they have ability to produce slime and biofilms whenever there is instrumentation at anatomical sites. However the significance of these isolates from urinary tract should be evaluated and treated accordingly.Rapid detection of a staphylococcal isolate especially 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 mec-A genes by molecular methods or PBP2A by latex agglutination test can be helpful for this purpose, provided they become more affordable to the patients[42].

Conclusion

MRSA is one of the most prevalent nosocomial pathogens worldwide. Healthcare-associated MRSA infections have recently declined in many countries throughout the world. However, infections caused by community-associated MRSA are becoming more prevalent in some areas. UTI due to *S. aureus* is a therapeutic problem. MRSA strains which are multidrug resistant (MDR) leaves very few options for treating UTI. Appropriate therapy should be based on the local antimicrobial susceptibility pattern for which periodic review of the antibiogram is essential. Drug resistance is a huge concern today and therefore, awareness about the rationale of judicious antibiotic use cannot be overemphasized. The limitations of our study include its retrospective nature which meant that causation was not addressed, and not all key information was available to study group.

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Conflict of Interest

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