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Full Length Research Paper

A study of the relationship between *staphylococcus saprophyticus* and urinary tract infection of women of childbearing age

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Coagulase negative *Staphylococcus* has long been considered of little significance as a urinary tract infection. The role of novobiocin resistant coagulase-negative *Staphylococcus saprophyticus* in infection of the urinary tract of women of childbearing age (14-40 years; mean age = 27 years; outpatients) was investigated. Three hundred female patients between the age bracket of 14 and 40 years (mean age= 27.3 years) attending University of Ilorin Teaching Hospital were consecutively sampled and 100 healthy women of the same age bracket were recruited as the control group. Of the 300 women recruited as the study group, 188 (62.7%) of them were positive for urinary tract infection of which 11 (5.85%) were positive for *S. saprophyticus*. This infection rate of 188 (62.7%) is statistically significant ($p<0.01$). In the control group, 30 (30%) of the 100 women were positive for asymptomatic urinary tract infection. The difference between the individuals positive for UTI in the control group and that of the study group is statistically significant ($p<0.01$). This study has been able to establish that *S. saprophyticus* and other coagulase-negative *Staphylococci* that are often previously dismissed as culture contaminants have greater influence in urinary tract infection especially among women of childbearing age.

Keywords: *Staphylococcus saprophyticus*; urinary tract infection; women of childbearing age.

INTRODUCTION

Coagulase negative *Staphylococci* have long been considered of little significance as a cause of urinary tract infections (Marrie et al., 1982; Mars, 2002). Several workers have however observed that some variety of coagulase negative *Staphylococcus* regarded as urine contaminants often cause serious urinary tract infection in patients (von Eiff et al., 2002; Michael et al., 2007). A particular species of coagulase Staphylococci characterized by novobiocin resistance was reported worldwide to be the second cause, after *Escherichia coli*, of cystitis and pyelonephritis in apparent healthy young women (Peggy et al., 1980; Sellin et al., 1980; Pfau, 1990). However, during the 1970s, a particular subgroup of coagulase negative *Staphylococci*, *Staphylococcus saprophyticus*, was shown to be an important cause of urinary tract infection in young females (Marrie et al., 1982) and has been reported to utilize Ssp and SdrI as virulence factors in the process (Kline et al., 2010). *S. saprophyticus*, a Gram-positive cocci remains an aetiology of uncomplicated urinary infections in both upper and lower urinary tract of young and middle-aged female outpatients (Kuroda et al., 2005; Burman et al., 1987). Uncomplicated urinary tract infection refers to infection in a structurally and neurologically normal urinary tract with abnormalities

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while complicated urinary tract infection refers to infection in a urinary tract with abnormalities. In general, infection in men, pregnant women, and children may be considered complicated while some considered upper tract infection as complicated (Bacheller, 1997; Ronald, 1997; Hooton, 2000). Unlike *S. epidermidis* infection which is hospital acquired, *Staphylococcus saprophyticus* infections are all acquired outside the hospital (Archer, 2000).

It is a notable uropathogen without the involvement of indwelling catheters. This organism is cultured infrequently from the genitourinary mucosa of young sexually active women, which is identified by clinical microbiology owing to its resistance to 5 µg novobiocin disc, though it rarely showed resistance to most other antibiotics (Kahlmeter, 2008). Novobiocin resistance is rarely found among many coagulase negative *Staphylococci* of other species that are grown from the urine (Etienne and Vandenesch, 2000; Diekema et al., 2001). Studies of female outpatients in Sweden and at the University of Florida and Washington found *S. saprophyticus* to be the cause of 3,230 and 11 percent of urinary tract infections, respectively, second to *E. coli* the cause of 65 to 85 percent of infections (Wallmark et al., 1978; Jordan et al., 1980; Latham et al., 1983; Ejaz et al., 2011).

In Nigeria, the organism has also been reported in studies observed in female patients in Yola and Zaria, Northern Nigeria (Abubakar et al., 2001). Women generally do not have a lot of problems with urinary tract infection until they become sexually active (Nocolle, 2008). Therefore, once adulthood is reached, the prevalence of bacteria increases in the female population (Sobel and Kaye, 2000). This study therefore examines and provides a baseline data in Ilorin, North-central Nigeria of the situation with a view to establishing the relationship between *S. saprophyticus* and urinary tract infection of women of childbearing age.

MATERIAL AND METHODS

Subjects

A total of 300 women of childbearing age (14-40 years) were enrolled into the study. The subjects were patients attending various clinics of the University of Ilorin Teaching Hospital, Ilorin; and approval was given by the Ethical committee of the hospital before the commencement of the study.

Collection and processing of samples

Mid-stream samples of clean-catch specimens of urine in sterile universal containers were consecutively obtained from each subject. Each urine sample was given laboratory ascension number prior to analyses. The samples were examined immediately or refrigerated at 4˚C and examined within 2-4 hours of collection.

Urine microscopy

The method of Kass et al. (1956) was employed. The urine samples were mixed and aliquots centrifuged at 5000 rpm for 5 min. The sediments were examined using both x 10 and x 40 objectives for epithelial cell and red blood cells, white blood cells (pus cells) using a sterile, clean slide. The pus cells were examined at high power field, only those containing five and above were considered pyuric.

Urine culture

Sheep blood agar (BA), MacConkey agar and Mannitol salt agar (MSA) were used for culturing the urine samples. A calibrated sterile platinum wire loop using the semi-quantitative method was used for the plating. It has a diameter of 4.0 nm diameter designed to deliver 0.01ml. A loopful of the urine sample was inoculated into duplicate plates of the selective agar. All plates were incubated at 37^0C aerobically for 24 h. Mannitol salt agar is a selective agar medium, which was used to isolate salt-tolerant Staphylococcal organism. Presumptive coagulase-positive *Staphylococci* produce colonies surrounded by bright orange-yellow zones on Mannitol salt with a reddish zone (Baker et al., 2001).

Generic Identification of the Staphylococcus spp.

Polymerase Chain Reaction (PCR) for generic identification (*Staphylococcus* spp.) was carried out following the method described by Morot-Bizot et al. 2003 and Martineau et al., 2001 using the following primers: TstaG422 (F) (5′-GGC CGT GTT GAA CGT GGT CAA ATC A-3′) and TStag765 (R) (5′-TIA CCA TTT CAG TAC CTT CTG GTA A-3′) with the amplicon size of 370 bp. The following PCR condition was followed: 3 min at 96 °C, 40 cycles of 30 s at 95 °C, 60 s at 55 °C, 30 s at 72 °C and a final extension of 3 min at 72 °C. Gel electrophoresis was run using 2.5% gel stained with ethidium bromide and 0.5 x TBE buffer. The positive control was *S. aureus* ATCC 25923 while nuclease free water was used as the negative control.

Antimicrobial susceptibility test
Identification of S. saprophyticus using 5 µg Novobiocin

The disc diffusion method of Bauer-Kirby was used to ascertain the sensitivity of the isolates to antibiotics (Barker et al., 2001). Antibiotics used were those for urogenital pathogens: Erythromycin (10 µg), Ciprofloxacin (5 µg), Gentamicin (10 µg), Nitrofurantoin (200 µg), Amoxicillin-Clavulanate (30 µg), Ofloxacin (10 µg), Ceftriazone (30 µg), Cefuroxime (30 µg), Novobiocin (5 µg). The resulting diameter of inhibition was measured.

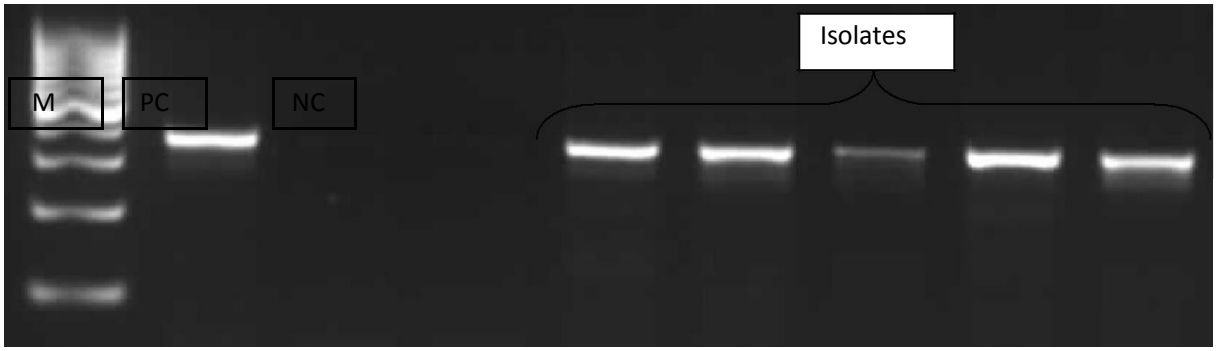

Figure 1. Gel Electrophoresis showing *Staphylococcus* spp. at 370 bp.
KEY: PC=Positive control, NC= Negative control, M= 100 bp Marker,

Table 1. Age distribution of women of childbearing age (14-40 years) attending UITH clinics (A) and healthy women of childbearing age (14-40 years) recruited as control (B).

Age (years)	A			B		
	№ examined	№ positive for UTI	% positive	№ examined	№ positive for UTI	%positive
14-20	39	20	6.7	10	2	2
21-25	59	50	16.7	24	6	6
26-30	119	74	24.7	44	15	15
31-35	52	31	10.3	13	7	7
36-40	31	13	4.3	9	-	-
Total	300	188	62.7	100	30	30

RESULTS

The result genus specific PCR based identification is shown below in Figure 1.

In this study, 300 urine samples were consecutively collected from women of childbearing age (14-40) who were attending the different clinics of University of Ilorin Teaching Hospital. Sixty-three of the samples were from the Maternity clinic, 98 from the General Outpatient Department (GOPD), 57 from the Gynecology Clinic, and 82 from the Medical Outpatient Department (MOPD). Of the 300 urine samples examined 188 (62.7%) were positive for urinary tract infection.The age range of the women of childbearing age attending the UITH Clinics between 14-40 years has a mean age of 27 years. UTI occurred with the highest proportion among women with age interval of 26-30 years with frequency of 74 (24.7%). This was followed by age interval 21-25 years with frequency of 50 (16.7%). The least frequency of individual with UTI was found at age interval of 36-40 years (4.3%). The infection rate of 188 (62.7%) in the study population is statistically significant (p<0.01) (Table 1).

Another group of individuals who are healthy women of childbearing age between the ages of 14-40 years were recruited as control (B). The mean age of this group is 27.3 years. However, the difference between the 30 (30%) individuals positive for UTI in the control group and that of 188 (62.7%) individuals positive for UTI in the study group in Table 1 is statistically significant (p<0.01) . The results from Table 2 (A) revealed that urinary tract infection occurred with highest proportion among the non-pregnant women in the age range of 26-30 years with a frequency of 45 (23.9%). This was followed by the 21-25 years with a frequency of 39 (20.7%). The least frequency of individuals with UTI among the non-pregnant women was found within the age range of 36-40 years with frequency of 5 (2.7%). Among the pregnant

Table 2. Occurrence of coagulase-negative *Staphylococcus* in the 188 female patients of childbearing age (14-40 years) positive for UTI (A) and Control (B).

Age (years)	Numbers positive due to coagulase-negative *Staphylococcus* spp.							
	A				B			
	Non-pregnant	Frequency (%)	Pregnant	Frequency (%)	Non-pregnant	Frequency (%)	Pregnant	Frequency (%)
14-20	2	1.1	-	-	-	-	-	-
21-25	3	1.6	-	-	-	-	-	-
26-30	6	3.2	3	1.6	3	10	-	-
31-35	3	1.6	-	-	-	-	-	-
36-40	2	1.1	-	-	-	-	-	-
Total	**16**	**8.6**	**3**	**1.6**	**3**	**10**	**-**	**-**

women, the age distribution of individuals positive for UTI is comparable to that of the non-pregnant women. UTI occurred with a high proportion in the age of 26-30 years unlike the 21-25 years of the non-pregnant individuals. However, the difference between the non-pregnant and pregnant women positive for UTI is statistically significant (p<0.01).

Table 2 (B) shows that the highest frequency of UTI occurred in the 26-30 age group in pregnant and non-pregnant control group. The difference between the non-pregnant and pregnant women in the control group positive for UTI is not statistically significant (p>0.01).

Coagulase-negative *Staphylococcus* occurred with the highest frequency among the UTI positive non-pregnant women with a frequency of 16 (8.6%) compared to that of pregnant women with a frequency of 3 (1.6%). However, the difference was not statistically significant (p>0.01, Table 3).

Coagulase –negative *Staphylococci* was isolated from 3 (10%) of UTI-positive non-pregnant women. The three women were in the 26-30 age group. None of the UTI-positive pregnant women had coagulase-negative *Staphylococci* (Table 2).

The result of novobiocin disc test revealed that *S. saprophyticus* occurred with higher frequency 11 (57.9%) compared to *S. epidermidis* 8 (42.1%). The difference is not statistically significant (p>0.01). It occurred more in non-pregnant women (52.6%) than in pregnant women (5.3%). The difference between the non-pregnant and the pregnant women was not statistically significant (p>0.01). The 21-25 and 26-30 age group showed the highest frequency of occurrence of *S. saprophyticus*. By comparison, *S. epidermidis* occurred in 6 (31.6%) and 2 (10.5%) of the UTI-positive non-pregnant and pregnant women, respectively. The difference in *S. epidermidis* among the pregnant* and non-pregnant individuals was statistically significant (p<0.01) (Table 4).

The frequency of detection of coagulase-negative *S. saprophyticus* and *S. epidermidis* among healthy women of childbearing age (14-40 years) recruited into the control group revealed that there was statistical significance (p<0.01) (Table 4).

Er-Erythromycin (10 µg), Ci-Ciprofloxacin (5 µg), Ge-Gentamicin (10 µg), Am-Amoxicillin-Clavulanate (30 µg), Ni-Nitrofurantoin (200 µg), Ofloxacin (10 µg), Ce-Cefuroxime (30 µg), Cr-Ceftriaxone (30 µg), R-Resistant, S-Sensitive.

Figure 2 shows the organisms isolated from the midstream urine of 188 women of childbearing age (14-40 years), that were positive for UTI; *S. aureus* occurred in the study group with the highest frequency of 37 (19.7.%) which is also similar to that of the control group with *S. aureus* having a frequency of 13 (43.3%). This is followed by *E. coli* 45 (23.9%), 5 (16.7%) both for the study group and control group respectively. *S. saprophyticus* occurred with a frequency of 11 (5.8%) in the study group and 2 (6.7%) in the control group. Among the study, *Enterococcus faecalis* has the least percentage with a frequency of 5 (2.7%). However among the study group, *S. epidermidis* and *Pseudomonas* has the least percentage with a frequency of 1 (3.3%) respectively.

Responses to questionnaire administered revealed the frequency with which the women change their sanitary pads; this is used to bring out the relationship between personal hygiene of the women and the occurrence of

Table 3. Sensitivity of *S. saprophyticus* to Antibiotics

Patients' Number	Antibiotics Discs/Sensitivity							
	Er	**Ni**	**Ci**	**Of**	**Ge**	**Ce**	**Am**	**Cr**
36	R	R	R	R	R	S	S	R
96	S	R	S	S	S	S	S	R
115	R	S	S	S	S	S	S	R
123	S	S	S	S	S	S	S	R
176	S	R	S	S	S	S	S	S
182	S	R	R	S	S	S	S	R
258	S	R	S	S	S	S	S	R
260	S	S	S	S	S	S	S	S
269	S	S	S	S	S	R	S	R
285	S	R	S	S	S	S	S	R
295	R	R	R	R	R	R	R	R
% sensitivity	72.7	36.4	72.7	81.8	81.8	81.8	90.9	18.2
Control group 23	S	R	S	S	S	S	S	R
59	S	R	S	S	S	S	S	R
% sensitivity	100	0	100	100	100	100	100	0

Er-Erythromycin (10 µg), Ci-Ciprofloxacin (5 µg), Ge-Gentamicin (10 µg), Am-Amoxicillin-Clavulanate (30 µg), Ni-Nitrofurantoin (200 µg), Ofloxacin (10 µg), Ce-Cefuroxime (30 µg), Cr-Ceftriaxone (30 µg), R-Resistant, S-Sensitive.

Table 4. Frequency of Detection of Species of Coagulase-negative *Staphylococcus* among the 19 cases positive for UTI (A) and Healthy Controls (B)

Age (years)	A				B			
	S. saprophyticus		***S. epidermidis***		***S. saprophyticus***		***S. epidermidis***	
	Non-pregnant	**Pregnant**	**Non-pregnant**	**Pregnant**	**Non-pregnant**	**Pregnant**	**Non-pregnant**	**Pregnant**
14-20	1	-	-	-	-	-	-	-
21-25	3	-	-	-	-	-	-	-
26-30	5*	1*	2	-	2	-	1	-
31-35	1	-	-	-	-	-	-	-
36-40	-	-	-	-	-	-	-	-
Total	**10(52.6%)**	**1(5.3%)**	**2(66.7%)**	**-**	**2(66.7%)**	**-**	**1(33.3%)**	**-**

UTI and *S. saprophyticus* among them. The difference between the proportions of individuals that have satisfactory hygiene compared to individuals with unsatisfactory hygiene in relation to change of sanitary

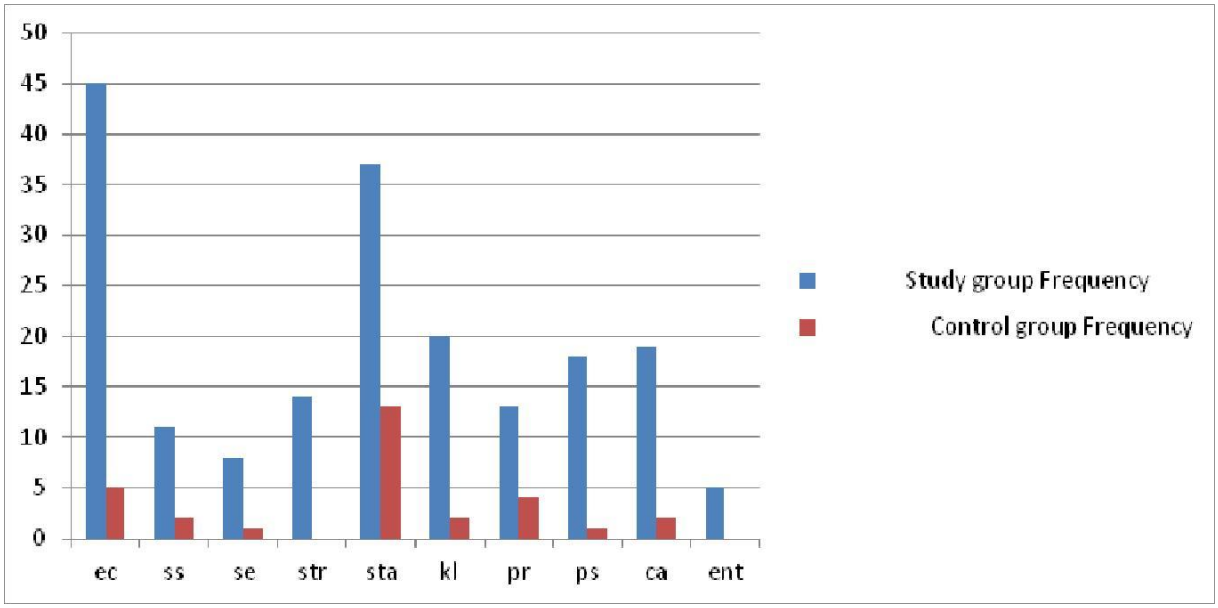

Figure 2. Frequency of urinary pathogens isolated from the Study and the Control Group.
Key: *Ec=Escherichia coli, ss= S. saprophyticus, se=S. epidermidis, str=Streptococcus spp.*, sta=*Staphylococcus aureus, kl=Klebsiella, pr=Proteus* spp., ps=*Pseudomonas* spp., ca=*Candida* spp., ent=*Enterococcus faecalis*

pads is statistically significant (p<0.01) Table 5 (A).

Table 5 (B) shows the correlation between particular modes of cleaning after defecation of women with isolation of *S. saprophyticus* positive for urinary. The front to back is described as a satisfactory cleaning method; the back to front cleaning is described as unsatisfactory. The difference between individuals that have satisfactory hygiene compared with individuals with unsatisfactory hygiene with respect to method of cleaning after defecation is statistically significant (p<0.01).

DISCUSSION

In this study, sheep blood agar was used because it assists in the rapid identification of pathogen and aids the study of hemolytic pattern of the organism. MacConkey agar was used because it assists in the identification of organisms that are lactose fermenters. It also provides a low electrolyte medium, which prevents most *Proteus species* from spreading. The prevalence figure is slightly lower than what has been reported by Marrie et al., (1982). In their work, 126 (86.9%) women were positive for urinary tract infection out of the 145 women in the study group. The highest prevalence of UTI in this study was found between the age ranges of 26-30 years with a frequency of 74 (24.7%). UTI has been reported by Latham et al. (1983) to be common within this age group because more women in this age bracket may be married and therefore are very sexually active. This pattern is similar to the observation of Mazzulli et al., (2001) who reported that young sexually active women were particularly prone to UTIs with an incidence of approximately 0.5 episodes per person per year. The control group (Table 6) also has similar distribution of women positive for urinary tract infection.

This study identified 63 (33.5%) of the 188 urinary tract infected women as being pregnant while 125 (66.5%) of them were non-pregnant. The highest proportion of those who were urinary tract infected but also pregnant was found within the 26-30 years age bracket. A slightly higher percentage (23.9%) of urinary tract infected but non-pregnant women was also with the 26-30 age group bracket. This result is comparable to those obtained in the study conducted by Abubakar et al. (2001) where women between the age bracket of 21-25 years had the highest percentage rate of 19.3%. A pregnant woman is an immune-compromised person. It has been reported by Chamberlain (2010) that the immune status of the pregnant women influenced their susceptibility to urinary tract infections. The frequency of isolation of coagulase-negative *Staphylococcus* was about the same among the patients (10%) as it was among the control healthy women. *S. saprophyticus* was found to be 90.9%

Table 5. Correlation of Frequency of Change of Sanitary Pads (A) and Methods of Cleaning after Defecation (B) with Isolation of *S. saprophyticus* from Urine of Women for Urinary Tract Infection.

	A	№of Individuals	Satisfactory	Unsatisfactory	№Positive for UTI	№Positive for *S. saprophyticus*	B	№of Individuals	Satisfactory	Unsatisfactory	№positive for UTI	№positive for *S. saprophyticus*
Study Group	**Once**	97		√	88(29.3%)	4(2.1%)	Front to back	266	√		165(55.0%)	4(2.1%)
	Twice	132	√		60(20.0%)	6(3.2%)						
	Thrice	71	√		40(13.3%)	1(0.5%)	Back to front	34		√	23(7.7%)	7(3.7%)
	Total	300			188(62.7%)	11(5.9%)	Total	300			188(62.7%)	11(5.8%)
Control Group	**Once**	24		√	15(15.0%)	- (0.0%)	Front to back	92	√		27(27.0%)	1(3.3%)
	Twice	66	√		13(13.0%)	2(6.7%)	Back to front	8		√	3(3.0%)	1(3.3%)
	Thrice	10	√		2(2.0%)	- (0.0%)	Total	100			30(30.0%)	2(6.6%)
	Total	**100**			**30(30.0%)**	**2(6.7%)**						

Table 6. Occurrence of UTI- positive women of childbearing age (14-40 years) (A) and healthy controls (B).

Age (years)	A				B			
	Non-pregnant		Pregnant		Non-pregnant		Pregnant	
	UTI	%	UTI	%	UTI	%	UTI	%
14-20	18	9.6	2	6.7	2	6.7	-	-
21-25	39	20.7	4	13.3	4	13.3	2	6.7
26-30	45	23.9	12	40	12	40	3	10
31-35	18	9.6	6	20	6	20	1	3.3
36-40	5	2.7	-	-	-	-	-	-
Total	**125**	**66.5**	**24**	**80**	**24**	**80**	**6**	**20**

sensitive to Amoxicillin-Clavulanate making it the most active antibiotic in this study. Furthermore, the organism showed a high resistance to Nitrofurantoin and Ceftriaxone. The resistance of the organism to Nitrofurantoin is similar to the findings of Wallmark et al. (1978).

Personal hygiene of women has been identified as a risk factor for acquisition of urinary tract infection. It has been established that poor personal hygiene following

urination and defecation may bring about infection of vaginal, especially when not handle hygienically. Bacteria secure nutriment for faster growth in tampons and sanitary pads wore for prolonged period of time.

From this study, it is recommended that bacteriological screening of urine samples for Novobiocin resistant coagulase-negative Staphylococcus should be sought for alongside with other uropathogens. Such approach is valuable for effective chemotherapeutic management of patients with UTI.

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