



BACTERIOLOGICAL PROFILE OF CATHETER ASSOCIATED URINARY TRACT INFECTION IN MEDICAL INTENSIVE CARE UNIT

Microbiology

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ABSTRACT

Background: Urinary tract infection (UTI) is the most common nosocomial infection among which more than 80% are catheter-associated (CAUTI)^[1]. As compared to patients in non-critical area, those in intensive care unit have more risk of acquiring CAUTI^[2,3]. **Objective:** This study was conducted to determine the bacteriological profile of catheter associated urinary tract infection in medical intensive care unit (ICU) patients and perform antibiotic susceptibility pattern of the isolated organisms. The risk factors associated with CAUTI was also determined. **Methods:** A total of 100 patients admitted in medical ICU and put on Foley's catheter were included in the study. They were followed up for the development of symptomatic CAUTI as per CDC guidelines. Urine culture, isolation and identification of organism were done by per standard microbiological methods. Antibiotic susceptibility testing was done by disc diffusion and MIC method following CLSI guidelines. **Results:** This study identified 26 CAUTI cases with 40 isolated organisms. Most isolates were from Enterobacteriaceae (34.5%) and non-fermenters (32.5%). *Pseudomonas aeruginosa* was the most common (25%), followed by *Klebsiella pneumoniae* (17.5%), *Enterococcus faecalis* (15%), *Escherichia coli* (15%), and *Candida* spp. (15%). High resistance was noted among Enterobacteriaceae, with 66.67% ESBL, 22.22% Amp C, 11.11% MBL, and 11.11% carbapenemase production. One methicillin-resistant *Staphylococcus aureus* was also isolated. **Conclusion:** The development of CAUTI is frequently observed in critically ill patients, with most cases being attributed to Gram-negative organisms. The rise of antimicrobial resistance is a global concern, with a growing number of multidrug-resistant strains causing CAUTI. To reduce the incidence of drug resistance, the prophylactic use of antibiotics should be avoided.

KEYWORDS

Catheter associated UTI, nosocomial, ESBL, MBL

INTRODUCTION

Healthcare associated infection (HAI) has emerged as an important health problem throughout the world, causing significant mortality and morbidity^[4]. Urinary tract infection (UTI) is the most common nosocomial infection accounting for 35%^[1] of the cases among which more than 80% are catheter-associated (CAUTI)^[1]. The patients admitted in intensive care unit have more risk of acquiring CAUTI compared to non-critical area.^[2,3]

Symptomatic CAUTI is considered when symptoms / signs consistent with UTI exists along with bacteriuria in a catheterized patient, provided the indwelling catheter was present for 48 hours or more before the development of signs and symptoms. If the catheter was removed after 2 days and the UTI criteria is fulfilled on the day of removal or the next day, then also it is considered CAUTI.^[5]

The source of infection in CAUTI can be endogenous or exogenous, with risk factors including female gender, old age, prolonged hospital stays and catheterization, impaired immunity, severe illness, diabetes, renal dysfunction, incontinence, and poor catheter care^[5,6]. CAUTI is caused by a wide spectrum of organisms ranging from Gram-negative bacilli to Gram-positive bacteria, and *Candida* spp. Frequent antimicrobial exposure leads to resistant organisms, making CAUTI a major reservoir of resistance. This increases the risk of cross-infections, prolongs hospital stays, raises healthcare costs, and ultimately results in higher morbidity and mortality.

This study was conducted to determine the bacteriological profile of symptomatic CAUTI and the antibiotic sensitivity pattern of the isolates including the resistance pattern in these isolates. The association of symptomatic CAUTI in relation to high risk factors was also determined.

MATERIALS AND METHODS

This cross-sectional study was conducted over one year (October 2014 to September 2015) at the Institute of Microbiology, Madras Medical College, in collaboration with the Medical ICU at Rajiv Gandhi Government General Hospital, Chennai. It involved 100 ICU patients aged 18 and above who were on Foley's catheter. Exclusion criteria included patients under 18, those catheterized before ICU admission, confirmed UTI on Day 1, or those whose catheters were removed or who were discharged before Day 3.

Informed consent was obtained from all participants. Data were collected using a structured questionnaire. Patients were examined daily for signs of urinary tract infection, and catheter care, including

daily meatal care with betadine or soap water and maintaining a closed drainage system, was closely monitored.

Urine specimens were aseptically collected from Foley's catheter, with at least 3ml placed in a universal container. Samples were sent to the lab within an hour. A Day 1 sample ruled out pre-existing UTI, with follow-up samples taken on Days 3, 5, 7, 10, 14, and then weekly until catheter removal, bacteriuria development, or patient discharge/death. Patients transferred to another ward were monitored for CAUTI symptoms for up to 48 hours.^[1]

The patients were diagnosed as symptomatic CAUTI as per CDC guidelines January 2014 which included the development of UTI with a bacterial count of $\geq 10^5$ CFU/ml on a specimen collected at least 48 hrs after hospital admission and a previous negative urine culture^[2].

A direct Gram's stain of uncentrifuged urine was performed to detect microorganisms, along with nitrite and leukocyte esterase testing using a dipstick. The urine was then centrifuged at 3000 rpm for 3-5 minutes, and a wet mount of the sediment was examined under 40x objective. More than 5 WBCs per high-power field (hpf) was considered significant for diagnosing CAUTI^[1,4].

Specimens were cultured using the semi-quantitative calibrated loop method on MacConkey and Blood Agar. Plates were read after 24 hours of incubation, with colony counts used to calculate microorganisms per milliliter. Plates with no growth or tiny colonies were incubated for an additional 24 hours. Isolates were identified based on colony morphology on 5% sheep blood agar, MacConkey Agar, and Gram staining.

Those colonies which showed GNB were further subjected to preliminary tests such as motility by hanging drop method, catalase and oxidase tests. The GNBs that were catalase positive, oxidase negative were suspected to belong to the family Enterobacteriaceae.

The GNBs which were catalase positive and oxidase positive were suspected of being non-fermenters. All these organisms were further speciated based on standard biochemical tests.

The *Pseudomonads* were speciated based on pigment production and additional biochemical tests such as gelatinase test, starch hydrolysis and xylose fermentation.

Colonies resembling *Staphylococci* and *Enterococci* were identified and speciated using standard methods and biochemical tests.

Kirby-Bauer disc diffusion method was used for antimicrobial sensitivity test and MIC by macrobroth dilution method was done for drugs meropenem and vancomycin.

The antibiotic discs used for Gram negative bacilli were ampicillin, amikacin, gentamicin, norfloxacin, nitrofurantoin, trimethoprim-sulphamethoxazole, cefotaxime, ceftazidime, tetracycline, piperacillin-tazobactam, imipenem and meropenem.

The antibiotic discs used for Gram positive cocci (*S.aureus*) were penicillin, amikacin, gentamicin, norfloxacin, nitrofurantoin, trimethoprim-sulphamethoxazole, ceftazidime and tetracycline. Those used for *Enterococcus* sp. included penicillin, tetracycline, norfloxacin, nitrofurantoin, vancomycin and high level gentamicin.

MIC by macrobroth dilution method was determined for the isolates that showed resistance to meropenem and vancomycin by disc diffusion method.

Detection of Extended Spectrum Betalactamase (ESBL)^[7]

Screening for possible ESBL production was done using cefotaxime (30µg) and ceftazidime (30µg) discs. Isolates with zone diameters ≤ 27mm for ceftriaxone and ≤22 mm for ceftazidime were confirmed by the ESBL phenotypic confirmatory test. A lawn culture of the test organism was made, and discs of ceftazidime (30µg) alone and ceftazidime plus clavulanic acid (30/10µg) were placed 30mm apart. An increase of ≥ 5mm in the zone of inhibition with the combination discs compared to ceftazidime alone indicated ESBL production.

Detection of Amp C beta-lactamases^[8,9,10]

Screening for Amp C beta-lactamase was done using ceftazidime (30µg) disc. A zone diameter of ≤18mm was suspected as Amp C betalactamase producer. Such isolates were further confirmed by Amp C disc test.

Detection of Metallobetalactamase (MBL)^[8,9,10]

Screening for MBL detection was done using imipenem (10µg) disc. Those isolates found resistant to imipenem were confirmed by imipenem EDTA combined disk test⁽³³⁾.

Detection of carbapenemase resistance^[7,9]

Those isolates which showed intermediate or resistant to one or more carbapenems (imipenem/meropenem) were tested for carbapenemase production by Modified Hodge test (MHT).

Detection of methicillin resistance *Staphylococcus aureus* (MRSA)^[7]

This was done using a ceftazidime disc (30µg) where A zone of inhibition ≤21mm was taken as mec-A positive and considered as MRSA.

Statistical analysis:

The primary outcome was the occurrence of symptomatic CAUTI. Personal (age, gender) and clinical parameters (disease type, steroid use, etc.) were considered explanatory factors. Descriptive analysis was presented as frequencies and percentages. Associations between variables were analyzed using odds ratios and 95% confidence intervals, with statistical significance assessed via chi-square test. Analysis was performed using Microsoft Excel and IBM SPSS version 21.

RESULTS

Among 100 patients, 26 developed symptomatic CAUTI, resulting in an incidence rate of 25.67 cases per 1000 catheter days. The majority (33%) were aged 18 to 30 years. Males made up 57% and females 43% of the study population. Most patients had catheter days ranging from 8 to 14 days (85%), with 11% having 1 to 7 days and 4% having 15 to 21 days. Catheterization was indicated for monitoring urine output in 96% of cases and for relieving urinary retention in 4%.

The descriptive analysis of all the potential risk factors for development of symptomatic was done. A total of 26 (26%) of participants were aged above 50 years. The proportion of subjects who had catheterization for more than 10 days was 43%. 17 % of subjects had Diabetes mellitus. The proportion of subjects, who were suffering from neurological, respiratory conditions, was 18% and 11% respectively. Only 5% of subjects were suffering from urological/nephrological conditions and 5 patients each had steroid use and other immunocompromised conditions. 3 patients each had

faulty catheter care.

Among the 26 (26%) of subjects who developed symptomatic CAUTI during the hospital stay, majority 19 (73%) developed it on 14th day, followed by 4(15.3%), who developed on day 10. Remaining 3(11.5%) subjects developed CAUTI on 21st day.

A total of 40 organisms were isolated these 26 CAUTI cases majority of which belonged to Enterobacteriaceae (34.5%) and non-fermenters (32.5%). *Pseudomonas aeruginosa* was the most common isolate (25%) followed by *Klebsiella pneumoniae* (17.5%), *Enterococcus faecalis* (15%), *Escherichia coli* (15%) and *Candida* spp. (15%). Other isolates were *Pseudomonas stutzeri* (5%), *Klebsiella oxytoca* (2.5%), *Pseudomonas fluorescens* (2.5%) and *Staphylococcus aureus* (2.5%).

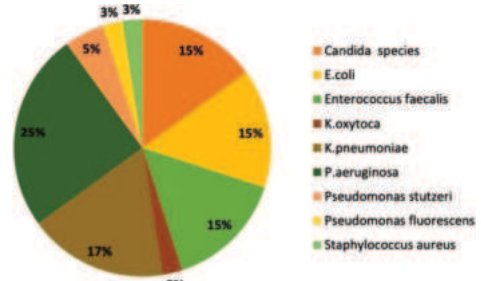


Fig 1: Distribution of organisms isolated in study group (N=100)

Among the 26 cases of CAUTI, 12 (46.15%) were monomicrobial infections and remaining 14 (53.84%) were polymicrobial infections.

Table 1: Distribution of organisms in polymicrobial infections

S.no.	Organism 1	Organism 2	Frequency
1	<i>Escherichia coli</i>	<i>Enterococcus faecalis</i>	1
2	<i>Klebsiella pneumoniae</i>	<i>Enterococcus faecalis</i>	1
3	<i>Pseudomonas aeruginosa</i>	<i>Candida krusei</i>	1
4	<i>Candida albicans</i>	<i>Enterococcus faecalis</i>	1
5	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas fluorescens</i>	1
6	<i>Escherichia coli</i>	<i>Candida parapsilosis</i>	1
7	<i>Pseudomonas aeruginosa</i>	<i>Candida tropicalis</i>	2
8	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas stutzeri</i>	1
9	<i>Escherichia coli</i>	<i>Klebsiella pneumoniae</i>	1
10	<i>Pseudomonas aeruginosa</i>	<i>Candida glabrata</i>	1
11	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>	1
12	<i>Pseudomonas aeruginosa</i>	<i>Escherichia coli</i>	2

Table 2: Distribution of organisms in monomicrobial infections:

S.no.	Organism	Frequency
1.	<i>Escherichia coli</i>	1
2.	<i>Klebsiella pneumoniae</i>	2
3.	<i>Klebsiella oxytoca</i>	1
4.	<i>Pseudomonas aeruginosa</i>	3
5.	<i>Pseudomonas stutzeri</i>	1
6.	<i>Staphylococcus aureus</i>	1
7.	<i>Enterococcus faecalis</i>	3

There was a high degree of resistance observed among Enterobacteriaceae.

However, they were commonly sensitive to piperacillin-tazobactam, imipenem and meropenem. Among *Pseudomonas aeruginosa* isolates, majority of them were sensitive to Imipenem (90%), meropenem (90%) and piperacillin-tazobactam (70%). Among *Pseudomonas stutzeri* and *P.fluorescens* isolates, all the isolates were sensitive to imipenem and meropenem. Only 50% of *Pseudomonas stutzeri* were sensitive to Piperacillin-tazobactam.

Table 3: Descriptive analysis of antimicrobial sensitivity pattern for Enterobacteriaceae in study group (N=14):

Drug	<i>Escherichia coli</i> (n=6)	<i>Klebsiella oxytoca</i> (n=1)	<i>Klebsiella pneumoniae</i> (n=7)
Ampicillin	0 (0%)	0 (0%)	*
Amikacin	0 (0%)	0 (0%)	0 (0%)
Gentamicin	1 (16.7%)	0 (0%)	0 (0%)

Nitrofurantoin	3 (50%)	1 (100%)	1 (14.3%)
Norfloxacin	0 (0%)	0 (0%)	1 (14.3%)
Cotrimoxazole	0 (0%)	0 (0%)	0 (0%)
Cefotaxime	0 (0%)	0 (0%)	0 (0%)
Ceftazidime	0 (0%)	0 (0%)	0 (0%)
Piperacillin- tazobactam	5 (83.3%)	1 (100%)	3 (42.9%)
Imipenem	6 (100.0%)	1 (100%)	5 (71.4%)
Meropenem	6 (100%)	1 (100%)	5 (71.4%)
Tetracycline	0 (0%)	0 (0%)	1 (14.3%)

*: intrinsic resistance

Table 4: Descriptive analysis of antimicrobial sensitivity pattern for Non-fermenters in study group (N=13):

Drug	Pseudomonas aeruginosa (n=10) N(%)	Pseudomonas stutzeri (n=2) N(%)	Pseudomonas fluorescens (n=1) N(%)
Amikacin	1 (10%)	0 (0%)	0 (0%)
Gentamicin	1 (10%)	0 (0%)	0 (0%)
Norfloxacin	2 (20%)	0 (0%)	0 (0%)
Cotrimoxazole	*	0 (0%)	0 (0%)
Cefotaxime	*	0 (0%)	0 (0%)
Ceftazidime	1 (10%)	0 (0%)	0 (0%)
Piperacillin-tazobactam	7 (70%)	1 (50%)	1 (100%)
Imipenem	9 (90%)	2 (100%)	1 (100%)
Meropenem	9 (90%)	2 (100%)	1 (100%)
Tetracycline	*	0 (0%)	0 (0%)

*: intrinsic resistance

Among 6 isolates of Enterococcus species 100% were sensitive for vancomycin. The proportion of isolates sensitive for nitrofurantoin, norfloxacin, tetracycline and high level gentamicin was 66.7%, 50%, 16.7% and 83.3% respectively. None of the isolates were sensitive to penicillin. Staphylococcus aureus isolate was sensitive to nitrofurantoin, tetracycline, vancomycin and linezolid.

Staphylococcus aureus isolate was sensitive to nitrofurantoin, tetracycline, vancomycin and linezolid and showed resistance to amikacin, gentamicin, norfloxacin, cotrimoxazole, cefoxitin and penicillin.

Among 27 isolates of Gram negative bacilli, 66.67 % for ESBL, 22.22% Amp C, 11.11 % MBL and 11.11% were positive for carbapenemase production. One Staphylococcus aureus was isolated which was methicillin resistant.

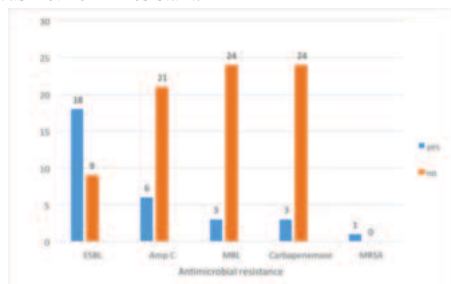


Fig 2: Antimicrobial resistance pattern of the organisms isolated

DISCUSSION

The rate of device associated infections shows variation in India. According to a study conducted by Angshuman Jana et al (2015)^[11], the incidence was 31.85%, study by Neha Garg et al (2015)^[12] found the incidence to be 20%, by Priya Datta et al (2014)^[13] found the CAUTI rate as 10.75% and 9.08/1000 catheter days, by Pooja et al (2014)^[14] as 32.14%, by Kamat et al (2009)^[15] as 33.6%, C.M.Poudel et al (2008)^[16] as 54% and Al Jebouri et al (2006)^[16] as 28.1%. In this study, out of 100 patients, 26 patients were diagnosed to develop symptomatic CAUTI during their course of hospitalisation. Therefore, the incidence was 26% and the CAUTI rate was calculated as 25.67 per 1000 catheter days.

The age distribution of the study subjects showed maximum proportion (33%) of the patients belonged to 18- 30 years. Males

constituted 57% and females 43% of the study subjects. In majority of the patients (85%), total catheter days were in the range of 8-14 days. The indication of catheterisation was found to be valid in all patients. Among 26 patients who developed symptomatic CAUTI, 19 developed in day 14.

A number of risk factors implicated with the development of symptomatic CAUTI were studied. The p value and Odd's ratio were calculated by Chi square test to find the statistical significance ($p < 0.05$) and the strength of association of these risk factors. Age ≥ 50 years showed increased development of CAUTI, the risk being 1.38 times. The incidence was also higher among females (34.88%) than males (19.3%). However, in this study age and gender showed no statistical significance. Similar results were seen in studies conducted by Priya et al^[13], Meric et al^[17] and Agrawal et al^[18].

Duration of catheterisation and length of hospital stay constitute an important risk factor and has been cited in studies by Priya Datta et al^[13] and Angshuman Jana et al^[11]. In this study, maximum patients (85%) belonged to the category of duration of catheterisation for 8 to 14 days. Among patients catheterised for 14 days, 86.3% developed CAUTI and among 4 patients catheterised till 21 days, 75% developed the infection. Duration of catheterisation $10 \geq$ days was found to be statistically significant as among 43 patients who had catheter for $10 \geq$ days, 60.47% developed CAUTI. This is due to the fact that the longer a patient stays in the ICU and catheterised, more are the chances that he will get colonised with multidrug resistant organisms present in the environmental niche. Faulty catheter care is another risk factor, but in this study it was not found to be statistically significant.

Co-morbidities have significant association with the development of CAUTI. In this study, diabetes had 5.98 times the risk, neurological causes 5.16 times, respiratory conditions such as COPD 6.44 times and those with urological/ nephrological causes had 13.27 times the risk. All these co-morbidities were statistically significant. These results are similar to study by Priya Datta et al^[13] where diabetes and COPD had significant association.

Infection by two organisms is common in CAUTI. In the study polymicrobial infection was seen in 53.84% and monomicrobial in 46.15 % of the cases, the predominant isolates being Gram negative bacilli (67%) among which Enterobacteriaceae were 34.5% and non-fermenters 32.5%. This finding was similar to other studies where in GNB constituted the common isolate: Neha Garg et al (80%)^[12], Priya Datta et al (72.61%)^[13] and C.M.Poudel et al (66.67%)^[16].

CAUTI-causing organisms vary by region and change over time. Tullu MS et al. (1998)^[19] found Escherichia coli as the most common, though Wazait et al. (2003)^[20] noted a decline, with Enterococcus spp. as the second most common. Taiwo et al. (2006)^[21] identified multiresistant Klebsiella spp. as the most common, followed by Pseudomonas spp., Escherichia coli, Staphylococcus aureus, Proteus mirabilis, and coagulase-negative staphylococci. Priya Datta et al. (2014)^[13] found Pseudomonas aeruginosa (35.7%) most common, followed by Enterococcus spp. and Klebsiella pneumoniae (15.4% each). Neha Garg et al. (2015)^[12] reported Escherichia coli (40%) as the most common, followed by Citrobacter koseri (20%) and Staphylococcus aureus (15%). Angshuman Jana et al. (2015)^[11] found Enterobacteriaceae, particularly Escherichia coli (19.4%), Pseudomonas spp. (19.4%), and Klebsiella spp. (16.6%), as the main pathogens.

In the present study, Pseudomonas aeruginosa was the commonest isolate (25%) followed by Klebsiella pneumoniae (17.5%), Escherichia coli, Enterococcus faecalis and Candida spp. (15%) each. P.stutzeri comprised 5% and Klebsiella oxytoca, P.fluorescens and Staphylococcus aureus 2.5% each. Among the gram positive bacteria, Enterococcus faecalis comprised 6 isolates and Staphylococcus aureus one isolate. There is an increasing trend of Enterococcus faecalis causing CAUTI.

Studies by Angshuman et al. (2015)^[11], Neha Garg et al. (2015)^[12], Priya Datta et al. (2014)^[13], and Chanda R. Vyawahare et al. (2015)^[22] have reported high antibiotic resistance among CAUTI pathogens. Catheterization increases the risk of UTI from highly resistant pathogens, with resistance patterns changing over time. In this study, Enterobacteriaceae showed high resistance to ampicillin, amikacin, gentamicin, nitrofurantoin, norfloxacin, cotrimoxazole, tetracycline,

cefotaxime, and ceftazidime. Sensitivity to piperacillin-tazobactam was higher: *E. coli* (83.3%), *K. oxytoca* (100%), *K. pneumoniae* (42.9%). All isolates were sensitive to imipenem and meropenem, except one *K. pneumoniae* isolate resistant to carbapenems. *P. aeruginosa* was mainly sensitive to piperacillin-tazobactam, imipenem, and meropenem. *E. faecalis* was 100% sensitive to vancomycin, 83.3% to high-level gentamicin, 66.7% to nitrofurantoin, and 50% to norfloxacin. Sensitivity to tetracycline was low (16.67%). One MRSA isolate of *S. aureus* was sensitive to nitrofurantoin, tetracycline, vancomycin, and linezolid.

Antimicrobial resistance is the main concern in healthcare associated infections because of the rapid increasing incidence. In this study, 66.67% of the GNB isolates were ESBL producers, 22.22% Amp C producers and 11.11% were positive for metallo-beta-lactamase and carbapenemase each. This finding was similar to the study by Mita et al (2013)^[23]. In another study conducted by Neha Garg et al (2015)^[12], ESBL production was found in 25% of the strains, 37.5% of the isolates were positive for Amp C production and MBL was detected in 18.7% of the isolates.

In the study, one *Staphylococcus aureus* isolated was MRSA and there were no vancomycin resistant enterococci.

CONCLUSION

Development of CAUTI is common in critically ill patients. Emphasis should be placed on good catheter management and reducing the duration of catheterization rather than prophylaxis in order to reduce the incidence of catheter-related UTI. Culture and susceptibility testing play an important role in the management of CAUTI.

The assessment of risk and need of catheterisation should be evaluated. The indwelling catheter should be used in the patients only if there is a valid indication. It should be removed when it is no longer indicated. If the catheter is required for more than 14 days, it should be replaced or alternative methods of catheterisation such as condom catheter, etc. should be considered. In catheterised patients, proper catheter bundle care should be followed.

Antimicrobial resistance is a growing threat worldwide. There is an increasing resistance to third generation cephalosporins among Gram negative bacilli. The prevalence of extended spectrum beta-lactamases, Amp C beta-lactamases and metallo-beta-lactamases constitutes a serious threat to current -lactam therapy leading to treatment failure. There is increase in the emergence of multidrug resistant isolates causing CAUTI. In order to decrease the incidence of drug resistance, prophylactic use of antibiotics should be discouraged. Knowledge of resistant pattern can help in implementing proper antibiotic therapy and infection control policy such as avoidance of overuse of antimicrobials, use of drugs for which pathogens are sensitive.

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