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Surveillance of acute community acquired urinary tract bacterial infections

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ABSTRACT

Objective: To record the antibiotic resistance of community acquired uropathogens over a period of 24 months (May 2011–April 2012).**Methods:** Urine samples from patients of outpatient department (OPD) were used for isolating urinary tract infection (UTI)-causing bacteria that were cultured on suitable selective media and identified by biochemical tests. Their antibiograms were ascertained by Kirby–Bauer's disc diffusion method, using 17 antibiotics of 5 different classes.**Results:** From 2137 urine samples 1332 strains of pathogenic bacteria belonging to 11 species were isolated. Two Gram-positives, *Staphylococcus aureus* and *Enterococcus faecalis* and nine Gram-negatives, *Acinetobacter baumannii*, *Citrobacter* sp., *Escherichia coli*, *Enterobacter aerogenes*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Proteus vulgaris* and *Pseudomonas aeruginosa* were isolated. Both *Staphylococcus aureus* and *Enterococcus faecalis* were vancomycin resistant, and resistant-strains of all pathogens increased in each 6-month period of study. Particularly, all Gram-negatives were resistant to nitrofurantoin and co-trimoxazole, the most preferred antibiotics of empiric therapy for UTI, but were moderately resistant to gentamicin, ampicillin, amoxycylav, ofloxacin and gatifloxacin. Most Gram-negatives produced extended spectrum β -lactamase.**Conclusions:** It was concluded that periodic surveillance of pathogens is an essential corollary in effective health management in any country, as empiric therapy is a common/essential practice in effective clinical management.

1. Introduction

Due to the lack of a rational antibiotic policy in clinical medicine, antibiotics are misused more often than not in developing countries and less often than not in developed countries, which lead to the increased emergence of multidrug resistant (MDR) strains of pathogenic bacteria and even of commensals. Not astonishingly, the MDR strains/serotypes of commensals too cause many a disease similar to well-known pathogenic bacteria, and have been spreading alike both in community and hospital settings^[1], unseen in the pre-antibiotic era. For example, from clonal nexuses of the Gram-positive

(GP), *Staphylococcus aureus* (*S. aureus*), the well-known commensal of soft tissues of human body, the methicillin resistant *S. aureus* (MRSA) has emerged independently at diverse geographic zones and have escalated to all types of communities, which has been regarded as the ghoulish and intractable superbug in the health domain for its aggrandizement of multiple resistances, worldwide^[2]. Such *S. aureus* strains, marked as MDR-MRSA, are seen as the marauding silently violent pathogen of all types of wounds (surgical sites, burns, cut injuries and bedsores, etc.), as well as in urinary tract, causing initially controllable bacteriuria, and fatal bacteremia ultimately^[3,4], if any urinary tract infection (UTI) is neglected. Indeed, when *S. aureus* was simply a commensal without any drug resistance character, never it caused any clinical exasperation. Further, the upper respiratory tract infection and UTI are commonplaces of initial infection at any rural community^[5–7]. Moreover as reported often, several species of Gram-negative (GN) bacteria insinuate the urinary tract apart from MRSA; for instance, MDR *Pseudomonas aeruginosa* (*P. aeruginosa*) avatars were the notoriously active uropathogen,

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known from a previous surveillance work by our school and others too^[8,9]. Particularly, spread of any MDR bacterial strain is so fast that, a patient with any morbidity—be it may non-infectious, from a community intending to attend the outpatient department (OPD) of a hospital, carries insidiously one or other MDR pathogen, causing a nosocomial spread. Such spreads too occur at frenetic pace in less-unhygienic conditions^[7,10,11], causing an avalanche of MDR strains of a torrent of bacteria sometimes against whom, particular antibiotics were never used to bacteria that were seen as multi resistant^[2,12]. To state curtly, the spate of MDR bacteria have caused a complex picture of infection dynamics of any community or hospital today^[13], challenging the cleanly totem of any hospital, even of a developed country.

Resistance for the first line antibiotics creates circumspection in the mind of a clinician for treating any infection empirically. Obviously, high level antibiotics such as those belonging to second or third generation cephalosporin or any other advanced carbapenem, cefuroxime or imipenem or a few more are used empirically for the prophylaxis of UTI for success^[14]. Logistically, one from a higher generation antibiotic groups should not be prescribed initially, without the availability of the culture report of a clinical sample; on the other hand, if the empiric therapy fails in an UTI case, further complications, cystitis, urethritis, pyelonephritis and a grievous bacteremia thereafter would occur in the next few days ultimately, leading to fatality due to use of an older/lowbrow antibiotic in face of an unknown antibiotic resistance in the causative bacterium. It would not be out of place to cite here that the mortality rate from bacteremia was approximately 81% in 1973^[15,16], and 50% in 2006 due to MDR *P. aeruginosa* strains^[17], a potent UTI bacterium. Moreover, it has been recorded that one in every five women picked up UTI and 95% of UTI causing organisms developed infectious complications at the notch of urethra, leading to cystitis. In sexually active women, recurrent UTI is reported to be more frequent. Young, adolescent girls also develop cystitis or bladder infection by UTI causing organisms^[18]. UTIs are common in patients with diabetes mellitus (DM) too, as this condition alters the urinogenital system, letting space/niche for the survival of pathogenic bacteria.

Indeed, without any functional abnormality in the urinary tract, uncomplicated UTI occurs in patients in around 6 days for the development of symptoms, and 2.4 days additionally for comorbidities from initial cystitis leading to restricted activities^[19-21], as in about 95% of all systematic UTI infections, cystitis is the most common initial comorbidity^[22]. Thus, in the case of an UTI patient, the empiric therapy is a must, as at least 3 or 4 days are needed for the antibiotic profiling of bacteria from the urine sample. Another inherent problem while addressing an UTI episode with a newer/latest generation of antibiotic is the expression of acute gastroenteritis or maculopapular rash, which could be transient as side effects in elderly people, or acute side effects in children^[23]. To overcome these problems, deliberate surveillances of infection scenario at several zones are needed, when considered from angles of public health in a community, as MDR strains of bacteria evolve and spread far, wide and faster than imagined^[24].

With symptomatic UTI, a patient may have fever ≤ 38 °C with chills, headache, vomiting, or burning pain, frequency or urgency during urination, change of colour of urine or new flank

or suprapubic pain and tenderness^[10]. Obviously, these symptoms are gathered from a patient before the urine sample is given for culturing or any antibiotic is administered, empirically. In addition, a patient may have significant deterioration in activities required to carry out a normal life or the cognitive status. Bloody urine, foul smell or an amount of sediment are often reported from urine of symptomatic cases. However, these cited symptoms are usually seen with patients, who had a defective urine analysis with a negative result^[25]; it is the determinative cause of acute UTI complications. In addition, the test for pyuria is also considered as a criterion for UTI, but it is neither relatively predictive for bacteriuria nor is a categorical symptom for UTI of a woman in a community^[25]. The prevalence of asymptomatic bacteriuria is high in elderly patients^[26], but that also is not an independent predictor of mortality, notwithstanding its progress to bacteremia, because a timely effective treatment with certain newer generation of antibiotics has been associated with control^[27,28].

The alternate therapy for uncomplicated UTI includes nitrofurantoin or fosfomycin, routinely^[29]. *In vitro* studies on antimicrobial resistant patterns with routinely used antibiotics for urinary isolates of *Escherichia coli* (*E. coli*) were many^[30]. However, the emergence of MDR strains resistant to newer and potent antimicrobials has become commonplace making therapeutic options limiting to antimicrobials, carbapenems, colistin and fosfomycin. An updated knowledge on antimicrobial susceptibility of MDR UTI pathogens is of prime importance for thwart of issues of public health from UTI. This study elucidates that Enterobacteriaceae members are the predominant UTI causing pathogens, followed by GP cocci.

Diabetes mellitus (DM) has been a major source of clinical problems^[31,32]. It is consensus that, individuals with DM have increased risk of most severe community acquired infections—respiratory tract infections primarily, followed by UTI^[33].

However, when local factors of spread of infections could be identified and quantified under an effective medical surveillance system for this class of pathogens, due steps could be initiated for the abatement of pathogen spreads, as the continual wave of the emergence of armoured MDR uropathogens create a frightening or rather an exacerbating state of affairs in clinical managements, especially in females. The present study records community-acquired (CA) accounts of antibiotic resistance of egregious strains of a cohort of uropathogens, isolated from clinical samples of patients attending the OPD of a hospital, over a period of 24 months the most common, rather notorious MDR pathogens. This study gives information on the antibiograms of 11 strains of bacteria in a typical Indian teaching hospital, an exhaustive study rarely conducted from clinical samples OPD patients.

This Indian record should strengthen the epidemiological database of this vast sub-tropical country and would help fixing facilitation of quality improvement in clinical management at the community sector for the reduction in the cost of hospitalization, as well as in the reduction of morbidity and mortality in the women section due to both GP and GN MDR uropathogens. The pharmacy world too is anticipated to be benefitted by this and similar surveillance studies on subtle MDR pathogens all over, for an exactitude in the empiric therapy for the control of uropathogens. Moreover, the empiric therapy options for this disease would be well substantiated by this surveillance with a

cohort of 11 MDR uropathogens. Consequently, it would help prevent, a priori, the use of some low-brow antibiotic regimen, for the desperate lady-patients in an acute state of morbidity, dabbling with an UTI from MDR bacteria that might lead to the terminal bacteremia, by blood stream infection initiated through the UTI problem at least in immune-compromised ones.

2. Materials and methods

2.1. Isolation and identification of pathogenic bacteria

From patients attending OPD of IMS and Sum Hospital, 2137 urine samples yielded 1332 strains of pathogenic bacteria belonging to 11 species (two GP and nine GN bacteria) during the span of 24 months (May 2011–April 2013). All isolated bacterial strains [*S. aureus*, *Enterococcus faecalis* (*E. faecalis*), *Acinetobacter baumannii* (*A. baumannii*), *Citrobacter* sp., *E. coli*, *Enterobacter aerogenes* (*E. aerogenes*), *Klebsiella oxytoca* (*K. oxytoca*), *Klebsiella pneumoniae* (*K. pneumoniae*), *Proteus mirabilis* (*P. mirabilis*), *Proteus vulgaris* (*P. vulgaris*) and *P. aeruginosa*] were identified by standard biochemical tests and were maintained as axenic cultures in suitable media. Microbial Type Culture Collection (MTCC) strain of each bacterium was used as reference controls during identification.

2.1.1. Purification of GP cocci

For pure-cultures of GP cocci, catalase and coagulase tests were performed. The catalase test was done with a drop of 3% H₂O₂ that caused effervescence indicating the presence of catalase enzyme. For the coagulase test, a lump of a test organism was emulsified with a drop of normal saline water (0.89%) and a drop of human blood serum was added to the suspension; clumping of cells was observed within 10 s, for confirmation of the presence of bound coagulase enzyme. When a sample of GP cocci responded positively to both catalase and coagulase tests, it was confirmed as *S. aureus*. Further, catalase negative, alpha-haemolytic (partial or green haemolysis of erythrocytes) colonies were subjected to bile-esculin test. The bile-esculin medium contains esculin and peptone for nutrition, and bile to inhibit growth of GP bacteria, other than Group D streptococci or enterococci. Ferric citrate was added as a colour-indicator. Organisms, which split esculin molecules and use the liberated glucose to supply energy, release esculin into the medium. The free esculin reacts with ferric citrate in the medium to form a phenol-iron complex, which turns the agar-slant from dark brown to black. An agar-slant that was more than half darkened within 48 h of incubation was bile-esculin positive, for the confirmation of *E. faecalis*; but the alternative non-darkening of the agar was taken as the negative result^[34].

2.1.2. Purification of GN bacilli

For pure-cultures of GN bacilli, the following tests were done in succession along with the catalase test. (1) Oxidase test: A bacterial colony was rubbed onto a filter paper, impregnated with tetramethyl-p-phenylenediamine dihydrochloride and the dye indophenols; the zone of the filter paper turns blue/purple in the positive result, while the negative result is with no change of colour. (2) Indole test: To an aliquot of 5 mL 48 h old grown culture (test culture), an aliquot of 0.5 mL of Kovac's reagent (p-dimethylaminobenzaldehyde, isoamyl alcohol and HCl) was

added. A formation of a cherry-red or purple-red ring at the interface of the broth culture and the reagent indicated the indole production from tryptophan by the test culture. (3) Methyl red test (MR test): An aliquot of 5 mL sterile MRVP broth (peptone 7 g, glucose 5 g, potassium phosphate 5 g, pH 6.9, inoculated and incubated for 48 h at 37 °C) was prepared. To this culture, five drops of methyl red solution were added as an indicator. If the total solution turned red, the test was taken as positive for the formation of organic acids as products. (4) Voges-Proskauer test (VP test): To an aliquot of 5 mL sterile MRVP broth, a loopful of the test culture was inoculated and the mixture was incubated for 48 h at 37 °C. To this culture tube, 10 drops of VP I reagent (5% α -naphthol, in absolute alcohol) and 2–3 drops of VP II reagent (40% KOH solution) were added and the mixture was allowed to stand for 15–20 min for the reaction to complete. The positive result was the appearance of red colour of the mixture, i.e., production of a neutral product, acetoin from the fermentation of glucose by the organism, and alternately yellow colour production indicated the negative result. (5) Citrate test: The test culture was inoculated onto a slant of Simon citrate agar that was incubated for 48 h at 37 °C. The change of colour of agar from green to blue indicated that organism used citrate as the sole source of carbon. (6) Urease test: The test organism was inoculated onto a slant of Christensen's urea agar (peptone, glucose, sodium chloride, mono-potassium phosphate, urea, phenol red, distilled water, and at pH 6.8). The hydrolysis of urea yielding ammonia gas increases the pH that changes the colour of the medium from off-white to pink/orange, the positive result. (7) Triple-sugar-iron test (TSI test): Two or three drops of test broth culture were inoculated on TSI-agar slant and subsequently, a stab was made up to the butt of the slant. The tube was incubated at 37 °C for 48 h; the black colour appearance indicated the H₂S production. (8) Nitrate test: An aliquot of 5 mL of nitrite broth (peptone 5 g, beef-extract 3 g, KNO₃ 1 g and distilled water 1 000 mL) was inoculated with 1 drop of 24 h old broth test culture and was incubated for 48 h at 37 °C. From the development of red colour within 30 s of adding a few drops of the reagent A (α -naphthol 5 g in 1 000 mL of 30% acetic acid) and reagent B (sulphanilic acid 5 g in 1 000 mL acetic acid) the positive result was inferred. No colour change suggested the negative result^[34]. MTCC strain of each GP or GN bacterium was used as the reference control in each biochemical test.

2.2. Antibiotic susceptibility test

All bacterial strains including the standard MTCC strains of each bacterium were subjected to antibiotic sensitivity tests by the Kirby-Bauer's method/disc diffusion method, using a 4 mm thick Mueller-Hinton agar (HiMedia, Mumbai) medium^[9]. An aliquot of 0.1 mL of 0.5 McFarland equivalents, approximately from an exponentially growing culture was spread on agar for the development of lawn of a strain of a bacterium at 37 °C in a BOD incubator (Remi CIM-12S). Further, on the lawn-agar of each plate, 8 high potency antibiotic discs (HiMedia) of 17 prescribed antibiotics of 5 different groups were placed, individually at equal distances from one another. Plates were incubated for 18 h at 37 °C and were examined for size-measurements of zones of inhibition around each disc, following the standard antibiotic susceptibility test chart of Clinical Laboratory Standard Institute (CLSI) guidelines^[35].

3. Results

From OPD, a total of 2137 urine samples yielded 1332 strains of pathogens belonging to 11 species with two GP and nine GN bacteria, during the span of 24 months. In total, there were 157 strains of *E. faecalis*, 201 strains of *S. aureus*, 103 strains of *A. baumannii*, 68 strains of *Citrobacter* sp., 98 strains of *E. aerogenes*, 253 strains of *E. coli*, 146 strains of *K. pneumoniae*, 60 strains of *K. oxytoca*, 90 strains of *P. mirabilis*, 58 strains of *P. vulgaris* and 98 strains of *P. aeruginosa*. Thus, *E. coli* was the maximally isolated UTI causing bacterium, followed by, *S. aureus*, *E. faecalis*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*, *E. aerogenes*, *P. mirabilis*, *P. vulgaris*, and *K. oxytoca* (Table 1).

GP bacteria as medium to large, smooth, entire, slightly raised, creamy yellow, green/beta-haemolytic colonies on blood agar, positive to catalase and coagulase tests were confirmed to be *S. aureus*. Further, bile-esculin producing colonies, negative to catalase and coagulase tests were taken as *E. faecalis*, which produced grayish, round, small colonies without any haemolytic zones on blood agar. Further, the GN bacterium, *A. baumannii* was identified on colony characteristics on nutrient agar (NA), MacConkey (MC) agar and cysteine-lactose-electrolyte-deficient (CLED) agar and with results obtained from adopted biochemical procedures: it grew as colourless, smooth, opaque, raised and pinpoint colonies on NA, but as colourless, smooth, opaque, raised and non-lactose-fermenting (NLF) colonies on MC agar; it was found positive to catalase, VP and citrate tests, whereas negative to oxidase, indole, MR and nitrate tests. Similarly, *Citrobacter* sp. was identified by its colony characteristics on MC agar and results obtained from the nine biochemical tests; it produced light pink-coloured late-lactose-fermenting (LLF) colonies after an 48 h of incubation on MC agar; particularly, it was found positive to catalase, MR, citrate and nitrate tests, whereas negative to oxidase, indole, VP and urease tests. On the TSI, the bacterium produced both acid and H₂S gas during growth. Again, *E. aerogenes* produced white convex with gamma-haemolytic colonies on blood agar, and lactose fermenting (LF), and mucoid colonies on MC agar. From, biochemical tests, *E. aerogenes* was seen positive to catalase, citrate, VP and nitrate tests, whereas negative to oxidase, indole, MR and urease tests. On a TSI slant, it produced acid in slant and gas production in the butt. *E. coli* produced flat dry, irregular colonies on NA; LF, flat, dry, pink and irregular colonies on MC

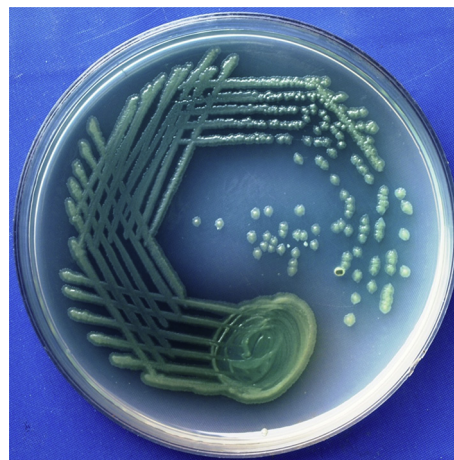


Figure 1. *Pseudomonas aeruginosa* on nutrient agar.

agar; purple coloured, flat, dry, irregular colonies, with metallic green colour on eosin methylene blue agar were noted by *E. coli*, but translucent blue colonies on CLED agar were evident. Further, *E. coli* was positive to catalase, indole, MR and nitrate tests, whereas found negative to oxidase, VP, citrate and urease tests; on the TSI test, it produced acid both in slant and butt with gas. Both, *K. pneumoniae* and *K. oxytoca* colonies on CLED agar were yellow and mucoid, whereas they produced LF, pink-coloured, mucoid colonies on MC agar. *K. pneumoniae* was found positive to catalase, VP, citrate and urease and nitrate tests, whereas it was negative to indole, MR and oxidase tests. On the TSI test, *K. pneumoniae* strains produced acids both in butt and slant along with gas production. *K. oxytoca* was found positive to the indole test, whereas the rest other test results were similar to those of *K. pneumoniae*. Similarly, both *P. mirabilis* and *P. vulgaris* had swarming and beta-haemolytic colonies on blood agar and translucent blue colonies on CLED agar. Further, *P. mirabilis* was found positive to catalase, MR, citrate and urease and nitrate tests, whereas it was negative to indole, VP, and oxidase tests. On the TSI test, *P. mirabilis* strains produced acids in both butt and slant along with H₂S gas. *P. vulgaris* was found positive to indole test, whereas the rest other results were similar to those of *P. mirabilis*. *P. aeruginosa* produced large, irregular, opaque colonies with blue-green pigment on NA (Figure 1); it was found positive to catalase, oxidase, urease and nitrate test, whereas negative to indole, MR and VP tests (Tables 2 and 3).

Table 1

Bacteria isolated from a total of 2137 urine samples of OPD patients.

Bacteria	May–October 2011	November–April 2012	May–October 2012	November 2012–April 2013	Total
<i>E. faecalis</i> ^a	25	45	45	42	157
<i>S. aureus</i> ^a	55	44	53	49	201
<i>A. baumannii</i>	25	28	21	29	103
<i>Citrobacter</i> sp.	14	21	15	18	68
<i>E. aerogenes</i>	21	28	23	26	98
<i>E. coli</i>	72	54	68	59	253
<i>K. oxytoca</i>	10	17	15	18	60
<i>K. pneumoniae</i>	38	37	33	38	146
<i>P. mirabilis</i>	23	24	15	28	90
<i>P. vulgaris</i>	19	15	13	11	58
<i>P. aeruginosa</i>	35	28	17	18	98
Grand total	337	341	318	336	1332

^a: Gram-positive bacteria, while the rest were Gram-negative bacteria.

Table 2

Media used for isolation and maintenance pathogenic bacteria from urine samples and their colony characteristics.

Bacterium	MTCC strain number	Media used	Colony characteristics
<i>E. faecalis</i>	439	Blood agar	Grey coloured, round, gamma hemolytic colonies
<i>S. aureus</i>	7443	Blood agar	Medium to large, smooth, entire, slightly raised, creamy yellow, with green/beta hemolytic colonies
<i>A. baumannii</i>	1425	Nutrient agar	As above without hemolytic activity
		Nutrient agar	Colourless smooth, opaque, raised and pinpoint
		MacConkey agar	Colourless smooth, opaque, raised, NLF
<i>Citrobacter</i> sp.	1658	CLED agar	Blue coloured opaque raised NLF
		MacConkey agar	Late LF light pink after 48 h
		Blood agar	White convex with gamma-hemolysis
<i>E. aerogenes</i>	2990	MacConkey agar	LF, mucoid
		Nutrient agar	Flat dry, irregular
<i>E. coli</i>	443	MC agar	LF, flat dry pink, irregular
		EMB agar	Purple coloured, flat dry, irregular colonies, with metallic green colour.
		Blood agar	Swarms on blood agar with beta-hemolysis
		CLED agar	Translucent blue
		MacConkey agar	LF, pink, mucoid
<i>K. oxytoca</i>	2275	CLED agar	Yellow mucoid
		MC agar	LF, pink, mucoid
<i>K. pneumoniae</i>	4031	CLED agar	Yellow mucoid
		MacConkey agar	LLF light pink after 48 h
<i>P. mirabilis</i>	NA	Blood agar	Swarms on blood agar with beta-hemolysis
		CLED agar	Translucent blue
		Blood agar	Swarms on blood agar with beta-hemolysis
<i>P. vulgaris</i>	1771	CLED agar	Translucent blue
		Nutrient agar	Large, irregular opaque with bluish green pigment

MTCC: Microbial type culture collection; CLED: Cysteine lactose electrolyte deficient; LF: Lactose fermenting; NLF: Non-lactose fermenting; NA: Not available.

Table 3

Biochemical identification of the isolated Gram-positive and Gram-negative bacteria.

Bacteria	Catalase	Oxidase	Coagulase	Indole	MR	VP	Citrate	Urease	TSI	Nitrate	Bile esculin
<i>E. faecalis</i>	–	Nd	–	Nd	Nd	Nd	Nd	Nd	Nd	Nd	+
<i>S. aureus</i>	+	Nd	+	Nd	Nd	Nd	Nd	Nd	Nd	Nd	Nd
<i>A. baumannii</i>	+	–	Nd	–	–	+	+	V	Nd	–	Nd
<i>Citrobacter</i> sp.	+	–	Nd	–	+	–	+	–	A/A H ₂ S	+	Nd
<i>E. aerogenes</i>	+	–	Nd	–	–	+	+	–	A/A	+	Nd
<i>E. coli</i>	+	–	Nd	+	+	–	–	–	A/AG	+	Nd
<i>K. oxytoca</i>	+	–	Nd	+	–	+	+	+	A/AG	+	Nd
<i>K. pneumoniae</i>	+	–	Nd	–	–	+	+	+	A/AG	+	Nd
<i>P. mirabilis</i>	+	–	Nd	–	+	–	+	+	K/A H ₂ S	+	Nd
<i>P. vulgaris</i>	+	–	Nd	+	+	–	+	+	K/A H ₂ S	+	Nd
<i>P. aeruginosa</i>	+	+	Nd	–	–	–	+	+	Nd	+	Nd

MR: Methyl red test; VP: Voges–Proskauer test; TSI: Triple sugar iron test; V: Variable; A/A: Acid in slant and butt; A/AG H₂S: Acid in slant and butt with H₂S gas production; A/AG: Acid in slant and butt with gas production; K/A H₂S: Alkali in slant and butt with H₂S gas production; Nd: Not done; +: positive; –: Negative.

All isolated bacterial strains were subjected to antibiotic sensitivity tests with 17 antibiotics used, in each 6-month period. Three aminoglycoside antibiotics, amikacin (30 µg/disc), gentamicin (10 µg/disc) and netilmicin (30 µg/disc) were moderately resistant to eleven species of pathogens used, in ranges, 27–76% of 157 strains of *E. faecalis*, 31–79% of 201 strains of *S. aureus*, 25–71% of 103 strains of *A. baumannii*, 19–71% of 68 strains of *Citrobacter* sp., 36–78% of 98 strains of *E. aerogenes*, 61–81% of 253 strains of *E. coli*, 45–65% of 60 strains of *K. oxytoca*, 66–79% of 146 strains of *K. pneumoniae*, 63–89% of 90 strains of *P. mirabilis*, 61–71% of 58 strains of *P. vulgaris*, and 66–86% of 98 strains of *P. aeruginosa*. Among these three antibiotics, gentamicin was recorded to be more resistant to these pathogens (Table 4).

Similarly, percentages of resistance patterns of isolated two GP bacteria with five antibiotics of the β-lactam group are

detailed (Table 5); resistance patterns were in ranges: 52–74% of 157 strains of *E. faecalis*, 61–82% of 201 strains of *S. aureus*. Likewise, GN bacteria were tested for four β-lactams only, with resistance patterns as given: 47–77% of 103 strains of *A. baumannii*, 52–71% of 68 strains of *Citrobacter* sp., 52–81% of 98 strains of *E. aerogenes*, 51–89% of 253 strains of *E. coli*, 58–81% of 60 strains of *K. oxytoca*, 54–83% of 146 strains of *K. pneumoniae*, 22–41% of 90 strains of *P. mirabilis*, 34–48% of 58 strains of *P. vulgaris*, and 41–75% of 98 strains of *P. aeruginosa*. For GN bacteria, antibiotics were resistant in the order: ampicillin > amoxycylav > piperacillin/tazobactam. But with GP bacteria such an order would be: amoxycylav > ampicillin > oxacillin > piperacillin/tazobactam (Table 5).

Further, resistance-percent values of UTI-bacteria to cephalosporin antibiotics (cefepime, ceftazidime and cefuroxime) in

Table 4

Percentage of resistance of all clinically isolated bacteria to three antibiotics of aminoglycoside group.

Bacterium	Amikacin (30 µg/disc)				Gentamicin (10 µg/disc)				Tobramycin (10 µg/disc)			
	I	II	III	IV	I	II	III	IV	I	II	III	IV
<i>E. faecalis</i>	55	67	76	64	47	56	59	54	27	34	41	39
<i>S. aureus</i>	69	76	79	71	57	59	56	58	31	49	56	54
<i>A. baumannii</i>	57	68	71	63	54	61	63	65	25	31	36	38
<i>Citrobacter</i> sp.	39	56	71	69	61	59	67	68	19	25	29	37
<i>E. aerogenes</i>	69	78	77	73	48	51	57	68	36	40	41	41
<i>E. coli</i>	74	76	81	79	76	79	80	78	61	67	65	69
<i>K. oxytoca</i>	45	53	61	65	45	54	57	61	63	64	61	63
<i>K. pneumoniae</i>	66	76	79	79	67	69	67	66	66	78	77	75
<i>P. mirabilis</i>	63	69	78	74	89	67	66	69	87	71	76	75
<i>P. vulgaris</i>	62	69	67	70	69	67	71	70	66	67	61	65
<i>P. aeruginosa</i>	74	77	76	72	86	77	67	68	76	68	66	67

I: May–October 2011; II: November 2011–April 2012; III: May 2012–October 2012; IV: November 2012–April 2013.

Table 5

Percentage of resistance of all clinically isolated bacteria to four antibiotics of β-lactam group.

Bacterium	Amoxyclav (30 µg/disc)				Ampicillin (10 µg/disc)				Oxacillin (1 µg/disc)				Piperacillin/tazobactam (100/10 µg/disc)			
	I	II	III	IV	I	II	III	IV	I	II	III	IV	I	II	III	IV
<i>E. faecalis</i>	62	67	70	74	52	68	69	72	59	67	71	72	53	66	71	69
<i>S. aureus</i>	71	77	82	79	68	74	76	77	66	67	76	74	61	79	75	78
<i>A. baumannii</i>	55	62	67	65	69	77	69	59	–	–	–	–	47	61	64	55
<i>Citrobacter</i> sp.	52	58	61	65	54	59	62	71	–	–	–	–	65	67	63	71
<i>E. aerogenes</i>	52	61	72	66	65	69	75	71	–	–	–	–	65	80	81	76
<i>E. coli</i>	78	82	89	86	62	71	78	75	–	–	–	–	51	57	58	55
<i>K. oxytoca</i>	58	62	70	68	74	79	81	80	–	–	–	–	63	71	73	79
<i>K. pneumoniae</i>	54	67	76	73	74	79	83	79	–	–	–	–	65	72	77	73
<i>P. mirabilis</i>	25	22	31	35	32	41	43	39	–	–	–	–	27	31	35	35
<i>P. vulgaris</i>	42	38	41	44	34	39	48	44	–	–	–	–	35	42	44	45
<i>P. aeruginosa</i>	68	70	75	74	55	54	67	65	–	–	–	–	41	47	51	53

I: May–October 2011; II: November 2011–April 2012; III: May 2012–October 2012; IV: November 2012–April 2013; –: Not used.

each 6-month phases were in ranges, 57–76% of 157 strains of *E. faecalis*, 51–76% of 201 strains of *S. aureus*, 45–64% of 103 strains of *A. baumannii*, 27–76% of 68 strains of *Citrobacter* sp., 52–72% of 98 strains of *E. aerogenes*, 75–88% of 253 strains of *E. coli*, 53–78% of 60 strains of *K. oxytoca*, 54–74% of 146 strains of *K. pneumoniae*, 32–49% of 90 strains of *P. mirabilis*, 36–46% of 58 strains of *P. vulgaris*, and 77 to 49% of 98 strains of *P. aeruginosa* (Table 6). All these three antibiotics were almost equally resistant to the isolated UTI pathogens, confirming the consistence in the production of extended spectrum β-lactamase (ESBL) by majority of isolates.

Similarly, resistance-percent values of UTI-bacteria to antibiotics of the fluoroquinolone group (gatifloxacin, levofloxacin, ciprofloxacin and ofloxacin) in four 6-month phases were in ranges, 51–76% of 157 strains of *E. faecalis*, 68–89% of 201 strains of *S. aureus*, 45–77% of 103 strains of *A. baumannii*, 47–68% of 68 strains of *Citrobacter* sp., 47–81% of 98 strains of *E. aerogenes*, 60–87% of 253 strains of *E. coli*, 44–65% of 60 strains of *K. oxytoca*, 58–81% of 146 strains of *K. pneumoniae*, 25–49% of 90 strains of *P. mirabilis*, 25–45% of 58 strains of *P. vulgaris*, and 54–81% of 98 strains of *P. aeruginosa* (Table 7). These antibiotics were resistant to UTI-pathogens in

Table 6

Percentage of resistance of all clinical isolated bacteria to three antibiotics of cephalosporin group.

Bacterium	Cefepime (30 µg/disc)				Ceftazidime (30 µg/disc)				Ceftriaxone (30 µg/disc)			
	I	II	III	IV	I	II	III	IV	I	II	III	IV
<i>E. faecalis</i>	62	67	70	73	57	65	76	75	57	65	67	72
<i>S. aureus</i>	54	67	76	72	51	59	62	65	51	59	62	68
<i>A. baumannii</i>	45	52	57	58	52	55	61	64	52	55	59	62
<i>Citrobacter</i> sp.	56	67	76	64	47	56	59	54	27	34	41	39
<i>E. aerogenes</i>	62	70	72	69	52	57	63	67	52	57	53	56
<i>E. coli</i>	75	82	88	86	79	79	88	87	79	79	78	76
<i>K. oxytoca</i>	53	58	61	68	67	69	67	66	66	78	77	75
<i>K. pneumoniae</i>	64	65	71	74	54	59	63	61	54	59	63	60
<i>P. mirabilis</i>	35	32	36	39	34	43	45	49	34	43	45	51
<i>P. vulgaris</i>	45	38	44	45	36	41	43	46	36	41	43	45
<i>P. aeruginosa</i>	65	71	77	77	49	61	68	65	49	61	68	69

I: May–October 2011; II: November 2011–April 2012; III: May 2012–October 2012; IV: November 2012–April 2013.

Table 7

Percentage of resistance of all clinical isolated bacteria to four antibiotics of fluoroquinolone group.

Bacterium	Gatifloxacin (5 µg/disc)				Levofloxacin (5 µg/disc)				Ciprofloxacin (5 µg/disc)				Ofloxacin (5 µg/disc)			
	I	II	III	IV	I	II	III	IV	I	II	III	IV	I	II	III	IV
<i>E. faecalis</i>	63	66	72	69	53	67	69	68	51	57	69	67	67	65	76	73
<i>S. aureus</i>	71	77	82	76	68	74	76	72	78	84	89	74	68	79	85	81
<i>A. baumannii</i>	48	54	59	59	69	77	59	54	45	52	61	77	62	67	74	71
<i>Citrobacter</i> sp.	53	58	61	68	47	52	56	54	56	61	65	57	56	54	56	61
<i>E. aerogenes</i>	47	52	51	57	65	69	75	74	72	78	81	69	52	61	63	59
<i>E. coli</i>	75	80	85	78	60	71	75	74	75	80	87	71	74	78	79	75
<i>K. oxytoca</i>	55	57	65	62	44	49	53	56	47	52	51	49	51	59	62	60
<i>K. pneumoniae</i>	58	62	70	68	74	79	81	80	63	71	73	79	60	68	72	72
<i>P. mirabilis</i>	25	31	29	33	37	45	46	43	35	38	45	45	31	45	47	49
<i>P. vulgaris</i>	32	38	41	45	34	39	42	41	25	34	37	39	35	37	43	41
<i>P. aeruginosa</i>	68	72	75	67	54	54	60	63	56	59	61	54	79	81	78	81

I: May–October 2011; II: November 2011–April 2012; III: May 2012–October 2012; IV: November 2012–April 2013.

the order: ofloxacin > gatifloxacin > ciprofloxacin > levofloxacin; the later one was newly introduced.

Lastly, detailed antibiograms of three stand-alone antibiotics, co-trimoxazole, nitrofurantoin, and vancomycin were recorded. Surprisingly, vancomycin 30 µg/disc was found resistance for 24 and 22% of strains of *E. faecalis* and *S. aureus*, respectively (Table 8). Nine GN bacteria were tested for two stand-alone antibiotics with resistance patterns as given: 45–64% of 103 strains of *A. baumannii*, 51–62% of 68 strains of *Citrobacter* sp., 52–72% of 98 strains of *E. aerogenes*, 75–88% of 253 strains of *E. coli*, 43–68% of 60 strains of *K. oxytoca*, 54–74% of 146 strains of *K. pneumoniae*, 32–49% of 90 strains of *P. mirabilis*, 36–46% of 58 strains of *P. vulgaris*, and 49–68% of 98 strains of *P. aeruginosa* (Table 8).

In a multicenter study from India, involving 5 hospitals of New Delhi, examining 531 samples from non-pregnant women in OPDs, there were only 6 bacteria with prevalence-percent values: *E. coli* (68%), *Klebsiella* sp. (16.9%), *Proteus* sp. (5.5%), *Enterobacter* sp. (5.3%), *Staphylococcus saprophyticus* (2.8%), *Enterococcus* (1.5%); GN bacteria were mostly susceptible to piperacillin/tazobactam (90%) and nitrofurantoin (66%), but all of them were sensitive to meropenem (a carbapenem)^[36]. A recent report on childhood UTI from Jamshedpur, India revealed that *E. coli* strains from urine samples were increasingly resistant to penicillin and cephalosporin groups, but those were susceptible to nitrofurantoin and levofloxacin, while cefoperazone-sulbactam was the most sensitive antibiotic to other bacteria, *Klebsiella*, *Proteus* and *Pseudomonas*^[37].

Table 8

Percentages of resistance of all clinical isolated bacteria to three stand-alone antibiotics.

Bacterium	Co-trimoxazole (25 µg/disc)				Nitrofurantoin (300 µg/disc)				Vancomycin (30 µg/disc)			
	I	II	III	IV	I	II	III	IV	I	II	III	IV
<i>E. faecalis</i>	62	67	70	73	–	–	–	–	17	15	21	24
<i>S. aureus</i>	54	67	76	72	–	–	–	–	11	19	22	18
<i>A. baumannii</i>	45	52	57	58	52	55	61	64	–	–	–	–
<i>Citrobacter</i> sp.	51	59	62	60	47	52	51	57	–	–	–	–
<i>E. aerogenes</i>	62	70	72	69	52	57	63	67	–	–	–	–
<i>E. coli</i>	75	82	88	86	79	79	88	87	–	–	–	–
<i>K. oxytoca</i>	43	51	53	59	59	61	65	68	–	–	–	–
<i>K. pneumoniae</i>	64	65	71	74	54	59	63	61	–	–	–	–
<i>P. mirabilis</i>	35	32	36	39	34	43	45	49	–	–	–	–
<i>P. vulgaris</i>	45	38	44	45	36	41	43	46	–	–	–	–
<i>P. aeruginosa</i>	65	71	77	77	49	61	68	65	–	–	–	–

I: May–October 2011; II: November 2011–April 2012; III: May 2012–October 2012; IV: November 2012–April 2013; –: Not used.

4. Discussion

In this surveillance, GP isolates *S. aureus* and *E. faecalis* were vancomycin resistant, and all GN isolates were resistant to nitrofurantoin and co-trimoxazole, the most preferred antibiotics of empiric therapy for UTI in this zone. Prevalence of resistant-strains of all pathogens increased in each 6-month period. Further, β-lactam antibiotics were resistant in the order: ampicillin > amoxycylav > piperacillin/tazobactam, for GN bacteria. But with GP bacteria such the order was: amoxycylav > ampicillin > oxacillin > piperacillin/tazobactam. Antibiograms of 11 bacterial strains clearly demonstrated that all those isolates were floridly MDR.

A less recent epidemiological survey on uropathogens causing uncomplicated cystitis was reported with 4264 female patients from nine European countries and Brazil during 2003–06 revealed that 10% *E. coli* isolates were resistant to three different classes of antimicrobials with decreasing resistance values, ampicillin (48.3%), trimethoprim sulfamethoxazole (29.4%), nalidixic acid (18.6%). But, fosfomycin (98.1%), mecillinam (95.8%) and nitrofurantoin (95.2%) were effective in the control of *E. coli*. Further, *P. mirabilis* was recorded more susceptible to β-lactams and less susceptible to other antibiotics. *K. pneumoniae* strains were intrinsically resistant to ampicillin, but comparatively less sensitive to mecillinam (88.8%), fosfomycin (87.9%), cefuroxime (78.6%) and nitrofurantoin (17.7%),

while *S. saprophyticus* was having the ESBL activity of CTX-M type^[38].

An Israeli study, over a 10-year period recorded that *E. coli* was the most prevalent and the most resistant pathogen, specifically with resistant to amoxicillin-clavulanate, ceftriaxone, cephalothin in uropathogens isolated from community^[39]. Another study from Israel described infection from the usually occurring bacteria *E. coli* and *Klebsiella* sp., which were resistant to amoxicillin-clavulanate (24%) and an initial empirical treatment with cotrimoxazole and cephalexin was recorded as inadequate in approximately one-third of the cases^[40]. Less recently, from a multi-locus sequence typing of important genetic lineage of *E. coli* from UTI patients of North-west England, it was recorded that *E. coli* strains with multi-resistance cause UTI infections and subsequently bacteremia in community, eventually leading to mortality^[41]. Further, young Dutch males had *E. coli*, whereas elderly males had *P. aeruginosa* as UTI infections; the susceptibility to amoxicillin (63%) and trimethoprim (70%) was low, while it was high towards fluoroquinolones (91%) and amoxicillin-clavulanate (90%)^[42]. In an Italian study, collected from 61 273 urine samples over a 22-month period, predominance of bacteria were with values as follows: *E. coli* (67.6%), *K. pneumoniae* (8.8%), *E. faecalis* (6.3%), *P. mirabilis* (5.2%), *P. aeruginosa* (2.5%). Females were more affected than males. In this region, oral susceptibility to antibiotics were as follows: fosfomycin (72.9%), trimethoprim/ sulfamethoxazole (72.9%), ciprofloxacin (76.8%), ampicillin (48.0%), and amoxicillin/ clavulanate (77.5%). The analysis on gender and age related CA-UTI data revealed the presence of a similar set of infection causing bacteria in almost urine samples, but *Streptococcus agalactiae* and *P. mirabilis* were additionally present in those from females^[43]. A less recent American survey recorded that cystitis and pyelonephritis account to 250000 individual cases, and repeated cases of pyelonephritis in children caused scarring of kidney, leading to the subsequent renal failure in an adult stage^[44]. Moreover, a recent American study revealed that UTI *E. coli* infections were food borne, which had been a matter of consternation both in paediatric as well as adult cases^[45].

In a report from Thailand, it had been recorded that from CA-UTI *E. coli* was the most predominant pathogen with ESBL-producing activity and the isolates were resistant to gentamicin (67%), cefotaxime (50%) and norfloxacin (50%)^[46]. In a Chinese report, it had been recorded that *E. coli* was the major pathogen in community CA-UTI cases, followed by *Enterococcus* sp. in Tianjin, China^[47]. Most recently from Chongqing, China, the prevalence of *P. aeruginosa* as the determinative agent CA-UTIs was recorded^[48].

A report on uropathogens from Kenya with pulsed-field gel electrophoresis demonstrated that *E. coli* strains resistant to fluoroquinolones and other commonly used β -lactam antibiotics had one of CTX-M-15 β -lactamase or CMY-2 or AmpC type of enzymes, and those caused major challenges in the management of UTIs^[49]. In a report from Madagascar of 903 pathogens from urine samples of males and females, it was recorded that there were 607 *E. coli* strains, 87 *Klebsiella* strains, 35 *S. aureus* strains, 30 *P. mirabilis* strains; most of those were resistant to amoxicillin, trimethoprim-sulfamethoxazole, ciprofloxacin, and were limitedly resistant to ceftriaxone and fosfomycin; but all those stains were sensitive to nitroloxline^[5]. In a Ugandan study, *Staphylococcus* (46.3%) and *E. coli* (39%) were reported as the most commonly isolated UTI bacteria, and those were resistant to co-trimoxazole (73.2%), nalidixic acid (52.4%) and

amoxicillin (51.2%). Since majority of those isolates were sensitive to gentamicin and amoxicillin-clavulanate, these antibiotics were suggested for the replacement of moribund drugs in empiric therapy^[7]. A Jordanian work recorded uropathogens, *Klebsiella* sp., *Proteus* sp., *Pseudomonas* sp. and *S. saprophyticus* occurring in the mention order in rural areas as the predominant pathogens; the need of frequent reevaluation of prevalence of UTI bacteria was emphasized^[50].

From the selected reports cited herein from different geographic zones along with the data recorded herein, it could be concluded that *E. coli*, followed by *Klebsiella* were the predominating UTI pathogens in most cases among GN bacteria, and *Staphylococcus* was recorded as the frequently isolated GP pathogen. All reported UTI bacteria were resistant to antibiotics that were in use, routinely. Re-scheduling of empiric therapy in treating UTI cases in most zones is required with an antibiotic from a higher generation. Moreover, in this zone in India, resistance of bacteria to the third generation cephalosporins and imipenem (carbapenem) is of clinical consternation that would be frequently met with any infection including the ones with UTI. Further, due to the short length of urethra in females, infection from fecal matter remains as a frequent possibility for UTI. For the control, a potent antibiotic is always a dire necessity in primary care hospitals in community of any developing country. Obviously, periodic surveillance of pathogens is an essential corollary in effective health management in any country, as empiric therapy is a common/essential practice in effective clinical management.

Conflict of interest statement

We declare that we have no conflict of interest.

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