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Original Research Article

Microbiological Profile and Antibiotic Resistance Patterns of Urinary Tract Infection in Geriatric Patients at a Tertiary Healthcare Center, Bhopal, India

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Abstract:

Background: Urinary tract infection s (UTIs) common affect elderly individuals and are among the most frequent indications for prescribing antibiotics in this population. Antimicrobial overuse is prevalent and can lead to negative consequences, such as developing multidrug resistant organisms.

Aim and Objective: To investigate the microbiological profile and antibiotic resistance patterns of urinary tract infections in geriatric patients.

Materials and Methods: This cross-sectional observational study included 200 elderly individuals receiving care at the Department of Medicine, Gandhi Medical College & Hamidia Hospital, Bhopal. Urine samples were collected and processed aseptically for analysis. The samples were inoculated on sterile culture media and processed using standard microbiological techniques. Antibiotic susceptibility testing was performed according to the Central Laboratory Standard Institute (CLSI) guidelines (2020).

Results: The mean age of patients was 68.54±7.2 years. Urinary culture revealed the growth of various micro-organisms in 37.5% of cases, while significant bacteriuria was documented in 26.5% of cases. Increased risk for UTI in geriatric patients was attributed to various risk factors e.g. prostate hypertrophy in males, post-menopausal changes in females, various co-morbidities like diabetes mellitus and physical limitations. Prostatomegaly was observed in 50% of total male patients with culture positivity and 30.6% of total patients with positive culture had diabetes mellitus.

Conclusion: *Escherichia coli* is the most common causative organism for UTI followed by *Klebsiella*. The commonly identified organisms demonstrate resistance to one or more antibiotics, with penicillins and cephalosporins being the most commonly resisted. However, the increasing prevalence of multidrug-resistant strainsis a growing concern when determining appropriate therapy for the management of UTI in elderly patients, in terms of effectiveness of existing antibiotics. Therefore, the antibiotics must be initiated cautiously with proper choice, dosage and duration of antibiotic when managing these cases.

Keywords: Urinary tract infections, Geriatric patients, Antibiotic resistance, *E.coli*, Bacteriuria

Introduction

The field of geriatrics is recognized as a distinct specialty in India as it has heterogeneous and complex health care needs due to co-existing medical, social, functional and psychological conditions [1,2]. UTI is an infectious disease that, while it can affect individuals of all genders and ages, is more commonly found in females.Urinary tract infections are among the most commonly observed infections among the elderly in bothgenders [3,4]. The increased risk of infection in elderly has been attributed to their deteriorating immune status, anatomical urinary tract abnormalities, cognitive impairment, poor hygiene, impaired local protective mechanisms, comorbidities (such as diabetes, steroid use, malignancy, and chronic debility), catheterization [5]. Other risk factors associated with UTI are urinary retention, high post void residual urine (PVR), previous UTI [6].

The diagnosis of UTI requires an appropriate constellation of symptoms, which may be localized to the urinary tract or outside it; identification of a recognized pathogen on culture; bacteriuria (more than 10^5 colony forming units CFU/mL); and evidence of white blood cells in the urine.The diagnosis of UTI requires the following four components:

1. Typical clinical symptoms of the urinary tract infection e.g. urinary urgency/frequency, dysuria, flank pain, suprapubic pain, fever, malaise; or acute onset of non-specific symptoms of infection in the absence of symptoms suggesting infection elsewhere.

2. Laboratory evidence of bacteriuria and pyuria (based on urine culture): Isolation of a urinary pathogen at $\geq 10^5$ CFU/mL in a freshly voided midstream urine specimen.

3. Systemic inflammation (e.g. fever/hypothermia, raised WBC or CRP).

4. The absence of another infection or non-infectious process to which the patient‘s symptoms can be readily attributed.

Urine culture is used to identify the type of organisms and their susceptibility to various antibiotics. Significant bacteriuria is usually considered if bacterial count is more than or equal to 10^5CFU/mL. Bacteriuria may be present even in asymptomatic patients, therefore the diagnosis of UTI cannot be solely based on a positive urine culture. The rate of ASB is much high in elderly, therefore bacteriuria alone cannot be considered an abnormal finding in older adults.

The causative organisms of UTI in elderly differ from usual UTI causing bacteria. Common causative agent for UTI among elderly in both the community and health care settings are *E.coli* followed by other members of Enterobacteraciae family (such as *Klebsiella* spp, *Proteus mirabilis* and *Providencia* spp). Other less common causative organisms of UTI in geriatric population are Enterococcus, methicillin-resistant *Staphylococcus aureus* [7,8]. Regarding the therapeutic options, management of UTI in geriatric population is often challenging as the choice and dosage of antibiotics must be paid special attention due to poor compliance, impaired drug absorption, concomitant medications secondary to comorbid conditions leading to drug interaction. Apart from this, secondary bacterial infection as well as diminished renal function must be taken in account while choosing the antibiotic [9,10].Urinary tract infection is one of the most common indication for prescription of antibiotics in elderly. It has been already demonstrated in some previous studies that 40–75% use of antimicrobials is inappropriate, particularly in the healthcare settings and its over-utilization is leading to negative consequences e.g. development of superbugs (multidrug resistant organisms), clostridium difficile infection and increasing burden of healthcare costs. Differentiating symptomatic UTI from asymptomatic bacteriuria (ASB) remains particularly challenging and treatment of ASB remains one of the commonest reason for which antimicrobials are prescribed.The present study at tertiary care centre investigates the microbiological profile (type of micro-organism and its species isolated on urine culture) of urinary tract infections in geriatric patients. It also assesses the antibiotic resistance pattern, a significant public health concern leading to increased morbidity, mortality, and hospitalization costs especially in geriatric population.

Materials and Methods

Study area and Patients

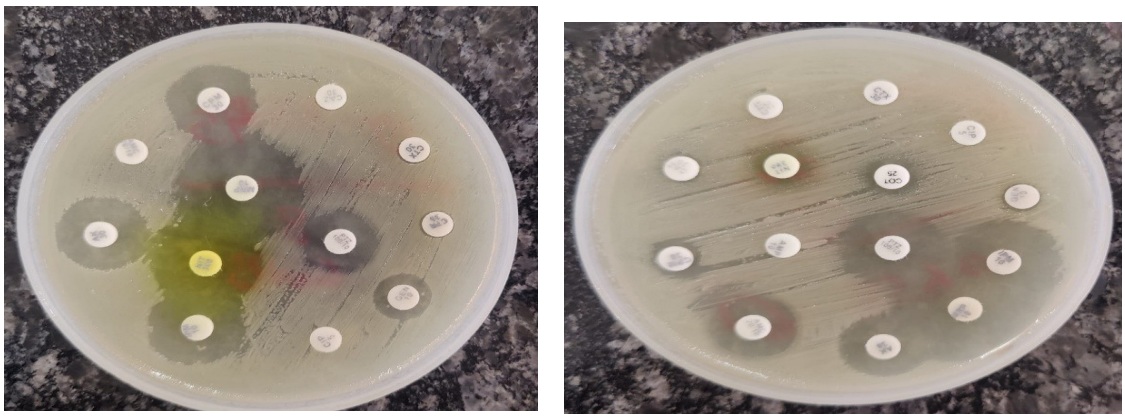
This observational cross-sectional study on individuals with age 60 years and above attending OPD(out-patient)and IPD(in-patient)of the Department of Medicine, Gandhi Medical College and associated Hamidia Hospital, Bhopal for 18 months i.e.,from January 2021 to June 2022. Patients already on antibiotic therapy, with an indwelling catheter, and immunocompromised status were excluded. Permission from Institute’s Ethical committee was taken initially[Ethics Committee Registration No. ECR/1055/Inst/MP/2018].All the patients fulfilling the inclusion criteria(age 60 years and above attending Department of Medicine, Gandhi Medical College and associated Hamidia Hospital, Bhopal) were enrolled after obtaining their written consent. The patient’s socio-demographic data, including age, gender, education, occupation and clinical history (symptoms, previous comorbidities, drug history andpersonal history) were registered.All the patients were then subjected to detailed physical examinations including general and systemic examinationfor various signs to ascertain the suspicion for UTI in those patients.

Urine Culture and Antibiotic Susceptibility Testing

Urine samples were collected(mid stream urine samples by clean catch method)and processed aseptically and inoculated on sterile culture mediausing streak plate method, and these media were further processed using standard microbiological technique [11].The antibiotic susceptibility testing was done using the Central Laboratory Standard Institute (CLSI) guidelines 2020 [12]. Patients were informed regarding further study plan and investigations needed.

[1a] [1b]

Image-1: Different Culture media showing growth of micro-organisms; 1a- Blood agar showing growth of gram negative organism; 1b- MacConkey agar media showing pink - coloured colonies of lactose fermenting bacteria.



[2a] [2b]

Image-2:Antibiotic susceptibility testing using disc diffusion method on Muller hinton agar showing zone diameters of different antibiotics.

Statistical Analysis

Data was collected in proforma and compilation was done using Ms-Excel. Data analysis was done with IBM SPSS Software version 20. Categorical variables were expressed as frequency and percentage whereas continuous variables were represented as mean and standard deviation.

Results

Two hundred geriatric patients seeking care at our institute were included in our study with mean age of 68.54±7.2 years. About 59% cases were males and 41% were females. Hypertension (41.5%) was the most common comorbidity, followed by diabetesmellitus (32%).

Urine culture revealed growth of varying micro-organisms in 37.5% cases whereas significant bacteriuria (>100000 CFU/ml) was documented in 26.5% cases. Out of all positive cultures (n=75), *E. coli* were observed in (n=25) 33.33% cases and 20% cases (n=15) had >100000 CFU/ml. Other bacteriawere *Enterococcus* (n=11) 14.66%, *Klebsiella oxytoca* (n=09) 12%, *Klebsiella pneumoniae* (n=09) 12%, MRSA (n=07) 9.33%, *Pseudomonas aeruginosa* (n=04) 5.33%, *Citrobacter*(n= 03) 4%, *Proteus vulgaris* (n= 03) 4% and *Staphylococcus* [CONS] (n= 01)1.33%. *Candida* species were found in4% (n= 03) of patients.

Among 75 cases of positive cultures, gram negative bacteria were isolated in 53 cases and gram positive bacteria were isolated in 19 cases. Majority of gram negative bacteria were resistant to cefotaxime (92.4%), ceftriaxone (88.6%), ceftazidime (86.7%), ciprofloxacin (73.5%), ampicillin (69.8%), amoxiclav (67.9%), cefipime (66%) and piperacillin-tazobactam (56.6%). Majority of gram positive bacteria were resistant to cefoxitin (100%), azithromycin (84.2%), ciprofloxacin (78.9%), penicillin (78.9%),cotrimoxazole (73.6%), clindamycin (73.6%), gentamicin (63%) and nitrofurantoin (52.6%)

Discussions

Urinary tract infections are commonly observed in geriatric population due to age associated changes

such as decline in immune functions, poor hygiene, urinary tract abnormalities, impaired local protective mechanisms, cognitive impairment, frequent catheterization and associated comorbidities [5]. The diagnosis of UTI is often difficult among elderly as they may present with non-specific symptoms such as weakness, loss of appetite, cough, disorientation [13]. Also, the prevalence of asymptomatic bacteriuria is reported to be higher among elderly [14].The present study was conducted on a total of 200 geriatric patients to study microbiological profile of urinary tract infection as well as to study antibiotic resistance patterns. Mean age of patients was 68.54±7.2 years and 59% patients with symptoms of UTI were males.

Urine culture is the gold standard method for growth and identification of bacterial pathogens responsible for urinary tract infection. For diagnosis of urinary tract infection, laboratory evidence of bacteriuria or pyuria on urine culture by isolating $\geq 10^5$ colony-forming units/ml of pathogen in a freshly voided midstream urine sample or growth of $\geq 10^3$ colony forming units/mL in catheter induced UTI [15]. Though $\geq 10^5$ colony-forming units/mL is described as a diagnostic criteria for diagnosis of UTI, however, lower level may also be relevant especially in patients with positive symptoms suggestive of UTI. The diagnosis of UTI cannot be relied solely on urinary culture in elderly as the incidence of asymptomatic bacteriuria is also high among them [15].

In our study, about 62.5% urine culture were negative in elderly with symptoms of UTI whereas urine culture was positive in only 37.5% of the patients. Of them, significant bacteriuria of more than 100000 CFU/ml was noted in 26.5% of total cases with symptoms of UTI. Among all positive cultures (n=75), the most common organism responsible for UTI in elderly was *E. coli*(n=25) (33.33%), followed by *Enterococcus* (n=11) 14.66%, *Klebsiella oxytoca* (n=09) 12%, *Klebsiella pneumoniae* (n=09) 12%, MRSA (n=07) 9.33%, *Pseudomonas aeruginosa* (n=04) 5.33%, *Citrobacter*(n=03) 4%, *Proteus vulgaris* (n=03) 4% and *Staphylococcus* [CONS] (n=01)1.33%.

Our findings were concurred with those of Eshwarappa *et al.*(2011), aimed to determine the presentation and risk factor associated with community acquired UTI. Of the total 510 patients included, 57% belonged to elderly age group,in which the most common organisms associated with UTI was *E. coli*(66.9%) [16]. Bagchi I *et al.*(2015) also reported *E. coli* (34.85%) as the most frequently isolated microbial agent causing UTI, followed by *Klebsiella* spp. (19.7%), *Pseudomonas* spp. (12.12%), *Candida* spp. (10.6%), *Enterococcus* spp.(6.06%), CONS (6.06%), *Staphylococcus aureus* (4.55%), *Citrobacter* spp.(3.03%), *Proteus* spp. (3.03%)[17].BeheraPK *et al.*(2016) also documented E coli (52.4%) and *Klebsiella pneumonie*(18.03%) as commonly isolated organisms in patients with UTI[5].In another study by Pugalendhi S *et al.(2019)*, *E. coli* (47.7%) was the most common cause of UTI in patients with CKD followed by *K. pneumoniae* (15.4%) [18].

According to the International Clinical Practice Guidelines (2019), nitrofurantoin is a drug of choice for management of uncomplicated UTI[19]. *E.coli* is the most common causative agent of UTI has low resistance to nitrofurantoin, but other bacteria may have intrinsic resistance to nitrofurantoin. Also, nitrofurantoin is contraindicated in patients with CKD: thus,nitrofurantoin, though least resistant cannot be given in all the cases. Resistance to antibiotics is increasing, so sensitivity testing is essential for effectively managing UTIs among older adults[11].Antibiotic susceptibility testing was done using CLSI guidelines 2020 [12]. Antibiotic susceptibility profile was done for gram positive as well as gram negative bacteria. We reported that most of the gram-negative bacteria were resistant to penicillins and cephalosporin group of antibiotics. The resistance is also developing against nitrofurantoin (52.6% cases), gentamicin (63% cases),amikacin (39.6% cases), and even to carbapenems. Gram positive bacteria were also resistant against azithromycin (84.2% cases), cefoxitin (100%), ciprofloxacin (78.9%), clindamycin (73.6%), cotrimoxazole (73.6%) and gentamicin (63%) in majority of the cases. However, only few cases showed resistant against doxycycline (21%), linezolid (10.5%), teicoplanin(21%) as well as vancomycin (21%).

In a study by Eshwarappa *et al*, the most common organism responsible for UTI in older people was *E. coli*, which showed resistance to extended spectrum beta lactamase (ESBL) inup totwo third of cases (n=340). Highest resistance was documented for fluoroquinolones whereas least resistance was documented for carbapenems[16]. BeheraPK *et al (2016)*reported low resistance for amikacinin common causative organisms of UTI. Colistin, Imipenem, Tigecycline, Teicoplanin & Amikacin were common antibiotics to which the common isolates [*E.coli, K. pneumonia and Enterococcus*] were sensitive. The total no.of subjects was 61 with age range of 60-85years. Average duration of hospital stay was 10.53 days and the death rate was 3.2%[5].Pugalendhi S *et al* (2019), studied clinical and microbiological profile of UTI in 65 CKD patients and the study reported *E.coli* and *Klebsiella* as the common causative agents of UTI and the sensitivity pattern revealed highest sensitivity for colistin, polymixin and carbapenem group [18].

Shanker M et al(2020)reported gram-negative bacteria to be more resistant to quinolones (ciprofloxacin resistance in72% cases of gram

negative isolates) and amoxicillin- clavulanic acid (68% cases of gram negative isolates). Gram negative bacteria were more sensitive for carbapenems(meropenem resistance in only 6% cases) and amikacin (12% cases). However, gram positive isolates were resistant to penicillin and quinolones [20].

Conclusion

Urinary tract infection is common among elderly individuals. Though urine culture is the gold standard method for detection of causative organisms and determining the choice of therapy by sensitivity testing, the incidence of asymptomatic bacteriuria is also high in elderly, probably due to impaired immune system. The most common causative organism for UTI is *E.coli* followed by *Klebsiella*. The common organisms are resistant to one or more antibiotics, most commonly to cephalosporin and penicillin group. However, the multidrug resistance is a growing concern in deciding the appropriate therapy for management of UTI among older people. Therefore, a cautious approach should be taken when initiating antibiotic therapy for these cases, considering factors such as the local resistance patterns, individual patient characteristics, and antimicrobial stewardship principles.

Limitation of Study

Urine culture has low sensitivity in the diagnosis of urinary tract infection. Therefore, it is essential to prioritize culture independent molecular techniques like next-generation sequencing and PCR, which have increased sensitivity and species diversity.

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Conflict of Interest

The authors declare that there are no conflicts of interest associated in this manuscript.

Table 1: Distribution according to socio-demographic variables and comorbidities

Age[years]	Frequency (n=200)	Percentage
61 to 70 years	151	75.5
71 to 80 years	32	16.0
>80 years	17	8.5
Sex		
Male	118	59.0
Female	82	41.0
Comorbidities		
Diabetes mellitus	64	32.0
Hypertension	83	41.5
COPD/Asthma	20	9.5
Stroke	19	9.5
Coronary artery disease	10	5.0

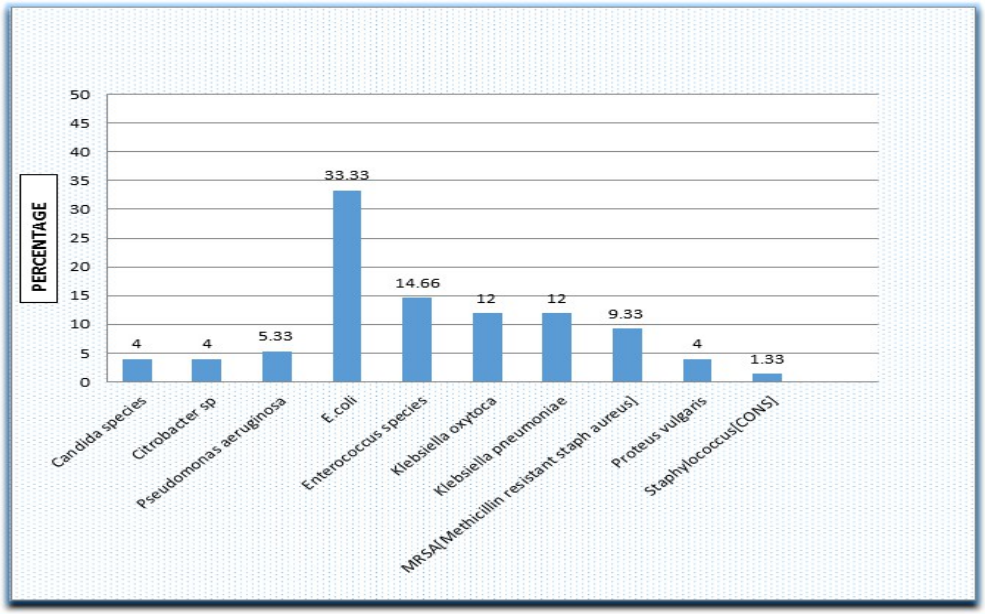

Figure 1- % Distribution according to findings of positive urine culture [n=75]

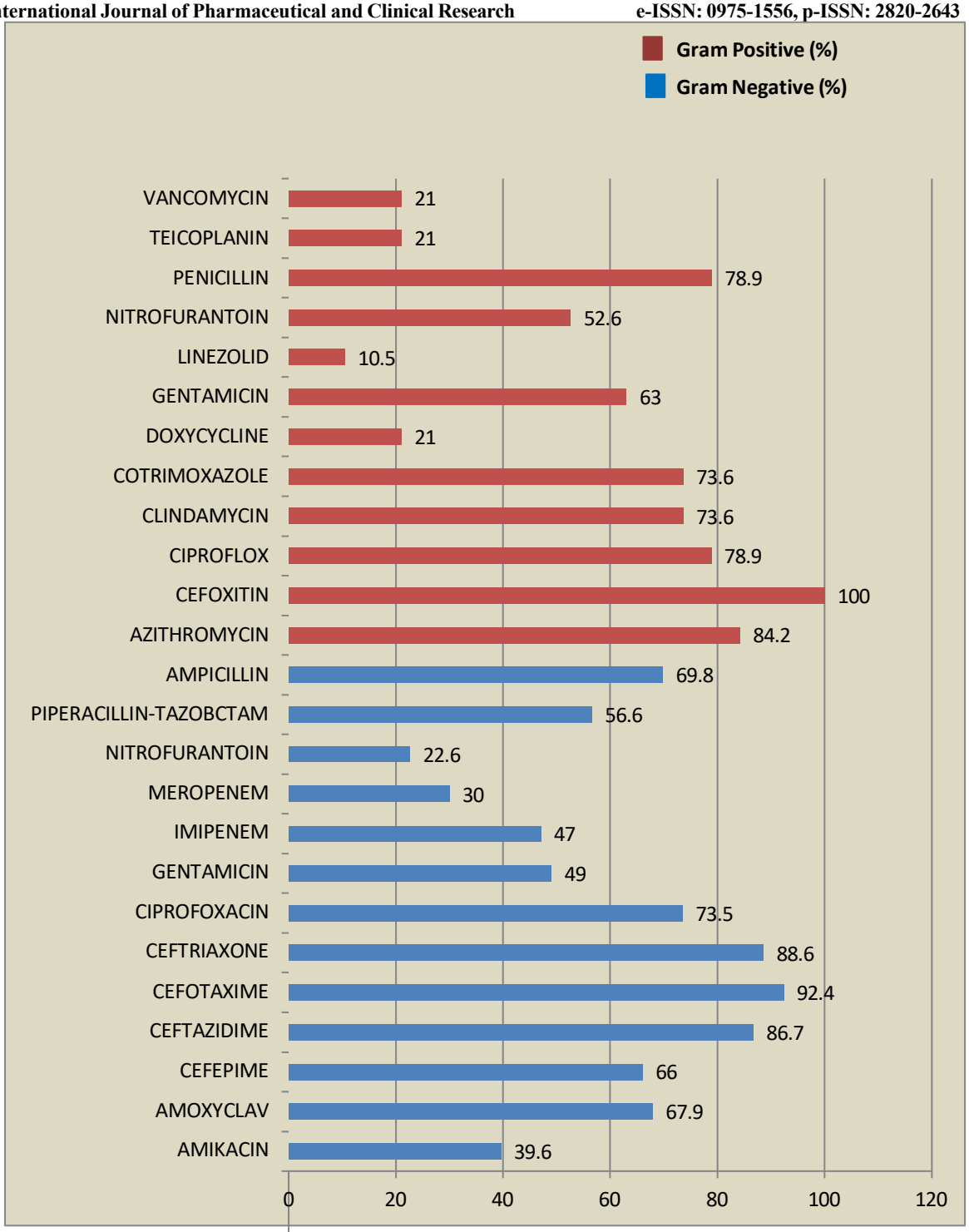
Gram Positive (%)
Gram Negative (%)
VANCOMYCIN 21
TEICOPLANIN 21
PENICILLIN 78.9
NITROFURANTOIN 52.6
LINEZOLID 10.5
GENTAMICIN 63
DOXYCYCLINE 21
COTRIMOXAZOLE 73.6
CLINDAMYCIN 73.6
CIPROFLOX 78.9
CEFOXITIN 100
AZITHROMYCIN 84.2
AMPICILLIN 69.8
PIPERACILLIN-TAZOBCTAM 56.6
NITROFURANTOIN 22.6
MEROPENEM 30
IMIPENEM 47
GENTAMICIN 49
CIPROFOXACIN 73.5
CEFTRIAXONE 88.6
CEFOTAXIME 92.4
CEFTAZIDIME 86.7
CEFEPIME 66
AMOXYCLAV 67.9
AMIKACIN 39.6
0 20 40 60 80 100 120

Figure 2: Antibiotic Resistance among Gram positive and Gram negative bacteria

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