Prevalence of uropathogen producing extended spectrum beta lactamase (ESBL) at urinary tract infection in chronic kidney disease patients

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INTRODUCTION

Urinary tract infection is one of severe public health problems worldwide. The most common causes of infections are either functional or anatomical abnormalities. These infections are common in all individuals, and ages.¹ This happens because the urethra not only serves as a passage for the outlet of urine but also serves as an entrance for the bacteria into the urinary tract.² Complicated UTI define as an infections which carry a risk of treatment failure as these typically require longer antibiotic courses and sometimes additional workup.² Complicated UTI incidence is associated with specific risk factors. For example, there is a 10% daily risk of developing bacteriuria with indwelling bladder catheters, and up to a 25% risk that bacteriuria will progress to a UTI.³

Simple UTIs in immune-competent females have been estimated to occur with as high a frequency as 0.7 infections per person per year. Fifty percent of females will have at least one UTI at some stage in life. Asymptomatic bacteriuria also tends to increase with age in females and is present in up to 80% of the elderly female population. It is rare among younger healthy males but can be present in up to 15% of older males.³ Most cases of urinary tract infections are due to the colonisation of the urogenital tract with rectal and perineal flora. The most common organisms include Escherichia coli, Enterococcus, Klebsiella, Pseudomonas, and other Enterococcus or Staphylococcus species.⁴ Of these, Escherichia coli is the most common followed by Klebsiella.⁵ Prevalence of E.coli was 28.7% and Klebsiella pneumonia was 16.2% in UTI as monoinfection.⁶

Epidemiological studies show an increasing number of patients worldwide suffering from chronic kidney diseases (CKD), which are associated with a risk for progression to end-stage kidney disease (ESKD).⁷ CKD patients stage 2–5, patients with regular chronic dialysis treatment (hemo- or peritoneal dialysis), and patients suffering from kidney allograft dysfunction are at high risk to develop infections, urinary tract infections...
(UTI) and/or sepsis (urosepsis). These groups show metabolic disturbance, chronic inflammation, and impaired immunocompetence. Escherichia coli is still the most common pathogen in UTI. A wide variety of other pathogens may be involved in UTI. Urological interventions, catheterization, as well as repeated courses of antibiotics contribute to an increased challenge of antimicrobial resistance. The diagnosis of UTI in CKD is based on standard clinical and laboratory criteria. Pyuria (≥10 leukocytes/µl) is more often observed in patients with oliguria and low bacterial colony counts. The aim of this study was to identify prevalence of the common uropathogen producing ESBL E.coli and K. pneumonia among the patient with Urinary Tract Infection (UTI) in Chronic Kidney Disease as well as the susceptibility of antibiotic therapy.

METHODS

This cross-sectional retrospective study to evaluate clinical urine isolates was collected from Prof. Dr. I.G.N.G. Ngoerah Hospital within July 2019 until July 2020. Identification and susceptibility tests in urine isolate were performed by Vitex-2 System (Biomerieux) and interpreted with CLSI 2020 standard. There are 1291 urine specimens from July 2019 to July 2020 in Microbiology Laboratory of Prof. Dr. I.G.N.G Ngoerah Hospital. We collected 210 urine specimens (16.26%) from patients with UTI in CKD, other urine samples with UTI (84%) during 12 months.

Inclusion criteria
(1) Urine samples were collected from patients with UTI in CKD (2) proper urine specimens for microbiology test. (3) urine culture positive for at least one bacterial strain.

Exclusion criteria
(1) Urine samples were collected from patients with diagnosis beside UTI and CKD (2) Renal transplant patients, (3) Patients on immunosuppressive therapy for any other primary systemic disease or primary glomerular disease, (4) sterile urine cultures.

Sample Processing
10 ml urine sample collected from ward and accepted in microbiology laboratory with a universal, wide-mouth, sterile, leakproof container. Urine sample cultured using Blood Agar Media and MacConkey Media then incubate overnight in 37°C. After 18 hour colonies were analysed from media. The colony count were enumerated as per the standard guidelines as significant (>10^5 cfu/ml), probably significant (1000-100000 cfu/ml) and insignificant (<1000 cfu/ml). Identification and susceptibility test bacterial strain were performed by Vitex-2 System (Biomerieux) and interpreted with CLSI 2020 Standard.

RESULTS
In this study female patients (68%) were more dominant than male patients (38%). From all ages group, 46 – 65 years were the most dominant risk in CKD with UTI (54%) followed by >65 years group (23%), 26-45 years group (14.3%), 12-25 years group (4.7%), 5-11 years group (1.4%), < 5 years group (0.9%). These patients were from non intensive care units (76%), intensive care units (19.5%) and outpatients (4.2%). From 1291 urine specimens, we collected 210 urine specimens with UTI (29%) from patients with UTI in CKD during 12 months.

Table 1. Characteristics of patient

<table>
<thead>
<tr>
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<tr>
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<tr>
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<tr>
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<tr>
<td>&gt;65 year</td>
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<td>23</td>
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<tr>
<td>No Catheter</td>
<td>24</td>
<td>11.4</td>
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</table>

Figure 1. Percentage of urine specimen from CKD patient with UTI
Prevalence of uropathogen in chronic kidney disease from urine specimens were E.coli (41.57%), K. pneumoniae (13.15%), and Pseudomonas aeruginosa (7.36%) and others (37.52%).

It was found that ESBL produced E. coli (56.32%) and also K. pneumoniae (54%), and the rest E. coli (43.68%) and K. pneumoniae (46%) not producing ESBL.

Bacteria of E.coli ESBL in patient with UTI and CKD almost (100%) susceptible to meropenem and amikacin, (96.6%) susceptible to tigecycline (93%) fosfomycin and 84% nitrofurantoin. The other antibiotics are less than (80%).

That antibiotics susceptibility E.coli ESBL at UTI patients with CKD showed different susceptibility with K. pneumoniae ESBL in UTI patient with CKD only susceptible to amikacin (92%), and meropenem (84.6%), and has low susceptibility to fosfomycin (65.4%), tigecycline (50%), and piperacillin/tazobactam (38.5%).

**DISCUSSION**

We have studied the clinical presentation, microorganisms and their antibiotic sensitivity pattern in 210 culture-proven urinary tract infections in the CKD population presenting to a tertiary care centre Prof. Dr. I.G.N.G. Ngoerah Hospital. Chowdury et al studied patients with urinary tract infection in Gujarat and found that the culture positivity was more in females compared to males. Females are more susceptible to infection than men. As anatomically position in female, had short urethra and closer position to the rectum. However, according to Shankar et al studied in Bengaluru, males were commonly affected and can be attributed to the increased incidence of CKD in males compared to females. In this study, from all chronic kidney disease, female patients were higher positivity in urinary tract infection compare than male patients. Prevalence of uropathogen UTI in chronic kidney disease at urine specimens were E. coli (41.57%), K. pneumoniae (13.15%), and Pseudomonas aeruginosa (7.36%) and others (37.52%).

Pugalendhi et al, studied from 65 CKD participants with UTI E.coli (47.7%) and K. pneumoniae (15.4%) were the most common isolates. This result similar to our study that showed E.coli (41%) and K. pneumoniae (13.15%). Study from Saudi Arabia found ESBL positive testing showed 296 (73.7% E. coli and 26.3% K. pneumonia) samples of positive isolates higher than our study. Number of sample and the time of study from Saudi Arabian can cause higher prevalence than in our study. Including numerous samples and
longer time of study can affect this. Our study showed that ESBL positive both E. coli (56%) and K. pneumonia (54%) had similar prevalence. Other studies showed that the isolated ESBL producing-uropathogens, E. coli were (82.2%) followed by K. pneumonia (17.2%). But the rate of ESBL-production was the highest in K. pneumonia (54.9%), followed by E. coli (42.5%).15,16

Ali et al suggested ESBL-producing uropathogens showed high resistance rate to most of the currently used antimicrobial agents such as co-trimoxazole (~70%), quinolones specifically ciprofloxacin and norfloxacin (>50%), but less resistant to other antibiotics such as gentamicin (38%) and much less resistant carbapenems such as ertapenem (0.6%) and meropenem (0%), amikacin (4.3%), nitrofurantoin (4.9%), piperacillin/tazobactam (0%) and fosfomycin (0%).14 This study found almost similar susceptibility in our study.

CONCLUSION
This research result of uropathogenic ESBL producers in patient UTI in CKD patient was E.coli 56.32%, that sensitive more than 80% in vitro to meropenem, amikacin, ticglycine gentamicin, fosfomycin, and nitrofurantoin. Also in patient UTI with CKD found that ESBL producers K. pneumoniae was 54% and sensitive more than 80% to amikacin and meropenem.

CONFLICT OF INTEREST
The authors affirmed that there were no conflicts of interest in this study.

FUNDING
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ETHICAL CLEARANCE
This study has obtained informed consent regarding isolates and clinical data for publication of this manuscript.

AUTHOR CONTRIBUTION
All authors contributed equally in this research and publication of this manuscript.

REFERENCES
6. Rezia RA, Vijendra R, Gopi A. Uropathogens Causing Urinary Tract Infection in Adults in a Tertiary Care Hospital. Published online 2020-9-14.