



Research Article

Prevalence of carbapenemase producing gram negative bacteria in renal failure urinary tract infection patients in Tikrit City, Iraq

Makarim Shteiwi Abed¹, Haider Rehman Alwan², Jaleel Najah Jaleel³

¹Salahdin Health Directorate /Higher Health Institute, Tikrit

²Diala Health Directorate Public Health laboratory, Baquba

³College of Health and Medical Techniques, Middle Technical University, Baghdad, Iraq

(✉) Corresponding Author: fi72523@gmail.com

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Abstract

The kidneys' ability to operate declines slowly and creatively as a result of chronic renal disease. It frequently results from issues with other serious medical disorders (such as spinal cord defects, hypertension, and diabetes). Due to the increased chances of acquiring end-stage renal disease (ESRD) patients, there is a higher incidence of multidrug-resistant organisms in the community, primarily methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *enterococci* (VRE). It is also poorly understood how gram-negative bacteria that produce carbapenemase affect ESRD patients on RRT (replacement renal treatment). 39 patients with urinary tract infections and renal failure participated in this study to determine the prevalence of gram-negative bacteria and Enterobacteriaceae that produce carbapenemase in Tikrit city. Disc diffusion method was used to determine whether the isolated and cultured bacteria were carbapenemase producing. According to the present study prevalence of carbapenemase producing group among renal failure patient with UTI was (78%), and not carbapenemase group was 22%. The females percentage was 40.6 % and male's percentage was 37.5%, recurrent UTI infections history for renal failure patients was very high 73% and in males 40% more than females 34%.

Keywords: Renal Failure, Carbapenemase Producing Bacteria, Recurrent

Introduction

An intentional and unorthodox reduction in kidney function is sparked by chronic renal failure. It frequently results from the side effects of more serious illnesses (such as hypertension, diabetes, genetic abnormalities, and spinal cord defects) (Reznichenko et al., 2012). Contrary to acute renal failure, which develops suddenly and severely, chronic renal failure develops gradually over years, months, or even days as the kidneys gradually stop functioning, leading to end-stage renal disease (ESRD), and the patient requires long-term management using renal replacement therapy (Levey et al., 2005). One RRT that removes waste products from the body, such as creatinine, urea, and extra water, is hemodialysis. The patients in the current research were in various stages of CKD,

but the majority were in stages 4 and 5, which are regarded as the latter phases, and they had RRT. Compromised innate and adaptive immune responses are linked to ESRD (Kato et al., 2008). In addition, bacterial overgrowth may arise from end-stage renal disease (ESRD), primarily in the duodenum and jejunum (Leblebicioglu et al., 2012). In addition to an increase in the number of bacteria in the gut, a rise in the number of potentially harmful bacterial families, including Enterobacteriaceae, is also seen. This takes place at the expense of the typical components of healthy gut flora, lactobacillaceae and prevotellaceae (Vaziri et al., 2013). Infections with multidrug-resistant organisms, primarily methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE), are more common in ESRD patients than in the general population as a result of

these increased opportunities for acquisition (Surel et al., 2014). CRE (carbapenemase resistant enterobacteriaceae) infections in ESRD patients on RRT (replacement renal therapy) are also poorly studied. In one case where gram-negative bacteria accounted for 52% of the infections, patients with ESRD on RRT had a 30-day death rate of 15.1% (Rojas et al., 2013). Patients not receiving RRT claim that ESRD patients receiving RRT have fatality rates for sepsis, pneumonia, and endocarditis that are two times greater (Eilertson et al., 2017).

For CRE-UTI, one research found that patients with renal failure who received RRT on average lived just one month longer than those in the regulator group who received the same treatment but were not infected (Bleumin et al., 2012). There are few reports in the literature of resistant Enterobacteriaceae pollutions in chronic RRT residents. Three-year research conducted in France on RRT patients revealed that 40% of them experienced bloodstream infections at some point throughout the investigation, and isolation of an MDR (multidrug-resistant) bacteria was associated with a higher risk of hospitalization or passing away (Fram et al., 2014). According to a different study, individuals with CRE infection had a higher fatality rate than those who have carbapenem-susceptible strains of the illness. Thirty-day mortality was linked to several coexisting conditions, such as chronic renal failure and dialysis, but they did not associate RRT and non-RRT patients with CRE infections (Hussein et al., 2013). infection with bacteria When Enterobacteriaceae were engaged in the widespread (74%) of the polluting microorganisms, of which (26%) were Enterobacteriaceae generating carbapenem, RRT patients in the United Kingdom saw poorer outcomes than bacterially ill renal transplant patients (Melzer et al., 2016). According to estimates, 72% of RRT patients have a uria after one year after starting their treatment, indicating that the variety of contamination between the two groups had a persistent negative impact on the UTI

rate (Shari et al., 2010). The risk of death is increased in individuals with renal failure who have CRE bacteria, pneumonia, or RRT who have UTIs caused by carbapenemase-resistant Enterobacteriaceae (Hauck et al., 2016). Although CKD has the potential to progress to end-stage renal disease (ESRD), it has previously been linked to cardiovascular problems earlier in the illness's course. Among the main causes of CKD are diabetes and hypertension, with age, smoking, and obesity serving as important confounders (Jha et al., 2013). A repeat UTI with resistive strain, trauma, stone formation, and renal disruption is a significant cause of CKD and acute kidney injury (AKI) (Maggi et al., 2012).

Materials and Methods

Thirty-eight individuals with renal insufficiency whose urine was suspected to contain UTI had samples taken. Patients were instructed to use a disinfectant to clean their external genitalia and to collect midstream pee in a sterile cap. Samples were transferred immediately to the microbiological laboratory while being stored in an ice bag. Physical examination (the obtained urine samples' characteristics of pH, color, volume, and appearance were examined). To find red blood cells, pus cells, germs, crystals, and other objects under a microscope. On nutrient agar, blood agar, and MacConkey agar medium, urine samples were cultivated before being kept at 37°C overnight. At least 105 colony-forming units CFU/ml of midstream urine was considered to be significant growth (Schmidt, 2016). Based on colony features, Gram staining, and a panel of biochemical responses, the isolates were classified as lactose fermenting or non-lactose fermenting Gram-negative bacilli (NFGNB) (microgen ID A+B panel test VITEK compact 2). According to recommendations from the Clinical Laboratory Standard Institute (CLSI) (Aswani et al., 2014), the Kirby Bauer's disc diffusion method was used to test the antimicrobial susceptibility of clinical isolates on Mueller-Hinton agar (O'Donnell et al., 2016).

Table 1. Clinical breakpoints for carbapenemases detection

Antibiotic	MIC 2010			MIC before 2010		Disc diffusion		
	S	I	R	S	R	S	I	R
Imipenem	≤ 1	2	≥4	≤ 4	≥16	≥23	20-22	≤ 19
Meropenem	≤ 1	2	≥4	≤ 4	≥16	≥23	20-22	≤ 19
Ertapenem	≤ 0.25	0.5	≥2	≤ 2	≥8	≥22	20-22	≤ 18
Doripenem	≤ 1	2	≥4	≤ 4	ND	≥23	20-22	≤ 19

By using the disc diffusion technique, isolates with reduced sensitivity to meropenem and imipenem (diameter of zones of inhibition 19 mm) were classified as belonging to the carbapenemase group (Aswani et al., 2014).

Results

According to the present study prevalence of carbapenem group among renal failure patients with UTI was 78% and the not carbapenem group was 22%, frequency for males and females was almost the same (12,13) respectively, as shown in Table 2

Regarding carbapenemase producing bacteria, the mostly isolated bacteria of renal failure with UTI was *E.coli* (52%) as shown in Fig 1. Followed by (16%) *Klebsiella pneumoniae* (8%) *Citrobacter diversus* and other isolated bacteria (4%).

According to the present study resistant to meropenem was very high 96%, imipenem resistant was 44% in comparison with non-renal failure UTI patients its considered very high (meropenem was 39%, imipenem was 10%) while imipenem

Table 2. Renal failure patients related to carbapenemase producing group

Group	Female		Male		Total	
	No.	%	No.	%	No.	%
Carbapenem group	13	40.63	12	37.50	25	78.13
Not-carbapenem	3	9.38	4	12.50	7	21.88
Total	16	50.00	16	50.00	32	100.00

Table 3. UTI duration of renal failure patients

Duration	Female		Male		Total	
	No.	%	No.	%	No.	%
Acute	3	7.89	3	7.89	6	15.79
Recurrent	13	34.21	15	39.47	28	73.68
Black	3	7.89	1	2.63	4	10.53
Total	19	50.00	19	50.00	38	100.00

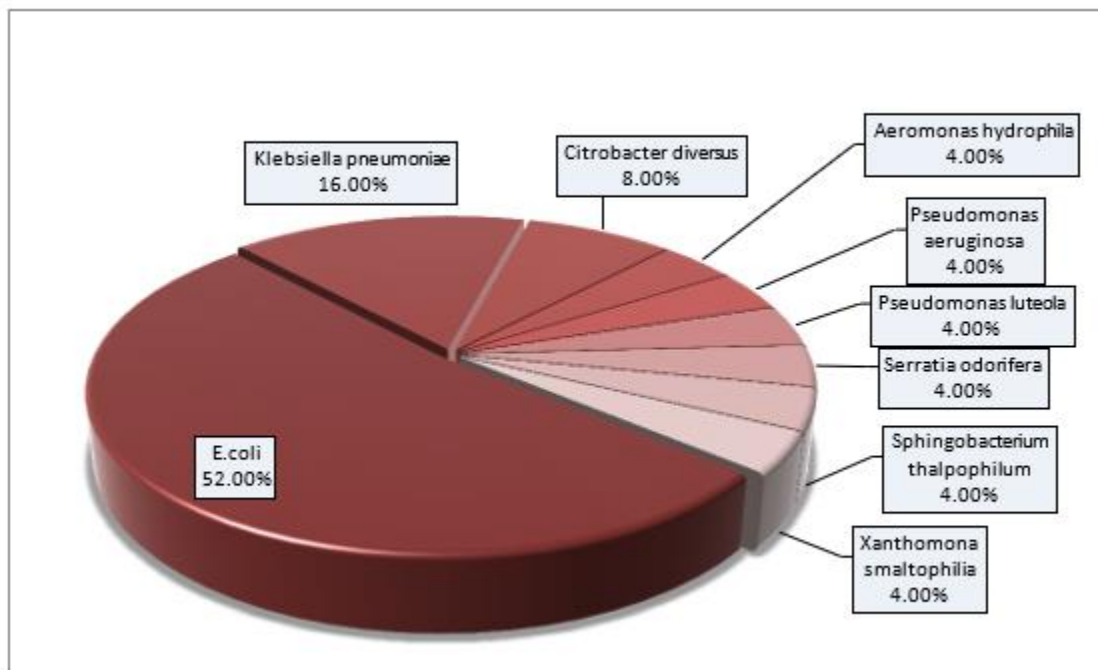


Fig. 1 Most isolated carbapenemase producing group bacteria in renal failure patients

intermediate susceptibility was 40% and meropenem was (4%) as Table 4 and 5 shown.

Discussion

According to (Bleumin et al., 2012) who also said that patients on RRT are more likely to die from antibiotic-resistant pathogens including MRSA and Clostridium difficile 20; the results of Table 2 support their claims. According to one study, individuals with CRE have an average survival time of one month of renal failure patients on RRT without infection

compared with more than 24 months for the control group of patients with renal failure (Pant et al., 2012).

As for carbapenemase-producing bacteria, the most isolated bacteria of renal failure with UTI was *E.coli* (52%) as shown in Fig 1. Followed by (16%) *Klebsiella pneumoniae* (8%) *Citrobacter diversus* and other isolated bacteria (4%), this almost agreed with (Bleumin et al., 2012) because it was the only study that included CRE in renal failure patients and his study included *Klebsiella* producing carbapenemase enzyme in hemodialysis patients and poorly outcomes of HD patients after infected with this organism.

Acute kidney injury (AKI) is a vital risk factor of CKD, which results from the recurrent UTI especially with “resistant strain, trauma, stone formation, renal disturbance” (Maggi et al., 2012). This agreed with our study and its result about recurrent UTI and renal failure and agreed with (Ateai et al., 2016; Pontillo & Mischak et al., 2016; Hill et al., 2016) as shown in Table 3

Table 4. Meropenem sensitivity test

Meropenem Sensitivity Result	Female		Male		Total	
	No.	%	No.	%	No.	%
Resistant	12	48	12	48	24	96
Sensitive	0	0	0	0	0	0
Intermediate	1	4	0	0	1	4
Total	13	52	12	48	25	100

Table 5. Imipenem sensitivity test

Imipenem Sensitivity Result	Female		Male			
	No.	%	No.	No.	%	No.
Resistant	6	24	5	20	11	44
Sensitive	2	8	2	8	4	16
Intermediate	5	20	5	20	10	40
Total	13	52	12	48	25	100

As Table 3 and 4 shown resistant to meropenem was high (96%) and for imipenem was (44%) meropenem was four to eight folds active on gram negative *enterobacteriaceae* than imipenem but less active on gram positive bacteria, imipenem is wide broad-spectrum antibiotic against aerobic and non-aerobic bacteria (Vading, 2016). Serious effect of carbapenemase producing gram negative bacteria was shown in treatment with resistant β -lactam antibiotics especially carbapenem group which causes many hypersensitivity reaction but most dangerous is neurotoxicity, nephrotoxicity, seizure on immunocompromised patients most of them imipenem (Pharmaceutical, 2007).

Conclusion

Carbapenemase producing enzyme gram negative bacteria; have high prevalence in renal failure patients whom historically undergo recurrent UTI. Most isolated Carbapenemase producing Enzyme bacteria was *E.coli* followed by *Klebsiella* spp. Serious effect of carbapenemase producing gram negative bacteria was shown in treatment with resistant β -lactam antibiotics especially carbapenem group which causes many hypersensitivity reaction especially seizure in immunocompromised patients (CKD).

Recommendations

Patient with UTI should have culture and sensitivity test to have proper antibiotic type especially immunocompromised

patients. Follow up childhood UTI patients and make sure of urine culture and sensitivity test with recording result are very important. Future study may have to focus on carbapenemase prevalence in different governments of Iraq. Ministry of health department may focus on educated population about antibiotics abuse and prevent pharmacists from giving antibiotics without physician permission or opinion.

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Conflict of Interest

The author hereby declares no conflict of interest

Consent for publication

The author declares that the work has consent for publication

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