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Screening and Characterization of Multidrug Resistant Bacteria from Chronic Kidney Disease Patients of Warangal

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With an overall incidence of over 10% within regular population, Chronic kidney disease is an issue that is becoming more and more important in terms of public health. The enhanced risk of infection, especially those brought on by bacteria that are multi-drug resistant, is one of the main side effects of chronic kidney disease. It is essential to screen and identify multidrug resistant bacteria in chronic kidney disease patients, especially those receiving haemodialysis, in order to prevent the transmission of these pathogens. Hence, to improve outcomes for chronic kidney disease patients, early diagnosis and prompt treatment of drug-resistant bacteria are essential. A total of 2219 samples were screened for antibiotic resistant microbes in hospital samples. 445 samples tested positive (20.05 %) for bacterial growth and 1774 samples tested negative (79.94 %). The rate of multidrug resistance bacterial infections was 17% and 43% higher in CKD patients for estimated glomerular filtration rate between 30 and 59 ml/min/1.73m2 and glomerular filtration rate 30 ml/min/1.73m2 respectively. Five bacterial isolates were found to exhibit multi-antibiotic resistance. The Multiple Antibiotic Resistance (MAR) Index ranged from 0.3 to 0.7 across the isolates. The isolates were identified as Enterobacter bugandensis, Enterococcus faecium, Providencia stuartii, Klebsiella variicola, and Escherichia coli by 16S rRNA gene sequencing and phylogenetic analysis. In conclusion, screening and identification of multidrug resistance bacteria is essential to prevent and control the spread of these pathogens and will be helpful for the effective treatment of the multidrug resistance in chronic kidney disease patients.

Keywords: Antibiotic; Chronic Kidney Disease; Estimated Glomerular Filtration; Multidrug Resistance Bacteria.

Millions of people globally are impacted by the global health issue known as chronic kidney disease (CKD). During time, there is a cumulative and permanent decrease of kidney function, which causes waste materials and fluid to build up in the body. In the ageing population, the increase in chronic diseases like diabetes and hypertension, as well as other variables including environmental pollution and lifestyle habits, are all contributing to an increase in the prevalence of CKD, which is correlated with substantial mortality and morbidity [1,2].

Recent research has demonstrated that CKD, which affects an estimated 10% of adults worldwide, is a serious global health issue[3]. By 2040, it is anticipated that CKD, would rank as

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the 5th leading cause of death globally[3]. Dialysis with CKD is a multifactorial disease with many risk factors, such as age, sex or race, genetic makeup, environmental exposures, and lifestyle choices. Also, it is a major contributor to coronary artery disease (CAD), heart failure, and stroke. It is also linked to a higher likelihood of other chronic conditions like diabetes, hypertension, and cancer[4]. Obesity, smoking, a poor diet, inactivity, and exposure to pollutants from the environment are other CKD risk factors[4,5].

Moreover, CKD can lead to mental decline, sadness, and a diminished standard of living[4]. Individuals with CKD frequently have impaired immune systems, making them more prone to bacterial infections. The rise in MDR has, regrettably, made it more difficult to treat these infections, which has increased the mortality and morbidity rates[6,7].

The MDR bacteria are those that are challenging to eradicate with traditional antibiotic therapy because they are resistant to a minimum of three distinct groups of antimicrobial drugs. CKD patients who have previously compromised immune systems and/or have had kidney transplants are at an increased risk of developing infections, making these germs a serious hazard to them[8]. According to previous studies, CKD patients had higher rates of MDR bacteria than the general population, with infections of the urinary tract representing the most common infection type[9].

A multidisciplinary strategy, including the utilisation of infection control procedures, antimicrobial stewardship programmes, and customised treatment plans, is necessary for the treatment of MDR bacteria in CKD patients. The MDR bacteria can spread among these patients, but the prudent use of antibiotics and the disease management to prevent infections, like hand cleanliness and correct catheter care, can assist[10,11]. In this study, we aimed to screen and identify multidrug-resistant bacteria from CKD patients undergoing dialysis besides exploring the impact of MDR bacteria on CKD patients with urinary tract infections (UTI). The aim of this study was to examine how MDR bacteria affect chronic kidney disease patients and the difficulties in controlling these infections.

MATERIALS AND METHODS

Sampling and study setting

During the research period, urine samples from 2219 patients with CDK who had undergone dialysis were obtained from 7 different dialysis centres in Warangal, Telangana State, India. Demographic details are shown in **Figure 1**. The samples were obtained between March 2018 and February 2019. Clear-catch mid-stream urine samples were collected from patients, both men and women with ages ranging from 20-65. The samples were taken in 2 ml sterilised screw-cap bottles, kept at 4°C, and then brought right away to the lab for further examination.

Renal function estimation

This study used electronic health records (EHR) and was an experimental approach. The goal of this study was to ascertain the prevalence of MDR bacteria and the incidence of antibiotic resistance among CKD admitted patients in dialysis centres of Warangal. Serum creatinine concentration and infections that were confirmed by microbial culturing at the time of hospitalization were taken into consideration for being included in the research. Patients receiving kidney replacement therapy who were also terminally sick were not included in the study. The estimated glomerular filtration rate (eGFR) of four major CKD Epidemiology Collaboration (KD-EPI) categories - eGFR 105, 60-104, 30-59, and 30 ml/min/1.73 m^2 was taken into consideration and compared for the reason that this range had the lowest infection risk and highest eGFR in an earlier study[12].

Isolation of bacteria from urine samples

On different media *viz,* blood agar, nutrient agar and McConkey agar, bacterial colonies were isolated using spread plate method. The samples collected were diluted by 10^4-fold using sterilized water and 0.1ml of ~~the~~ diluted sample was then spread quantitatively on petri plates having different media. The plates were finally incubated at 37p C for 24 h for the growth of bacterial colonies.

For this study, standard reference strains viz., *E. coli* MTCC-443, *K. pneumoniae* MTCC-4031, and *P. aeruginosa* MTCC-1688, procured

from the MTTC, IMTECH, Chandigarh were used in this present study.

Preparation of the test organisms for antibiogram profiling

Conforming to the guiding principles of the CLSI (Clinical and Laboratory Standards Institute), only 36 morphologically distinct bacterial colonies were evaluated for antibiotic sensitivity pattern by disc diffusion Kirby methodology on MH (Mueller-Hilton) agar[13]. Fresh bacterial culture in an aliquot of 0.1 ml and 0.5 McFarland was placed on MH agar and left to dry for 5 to 10 minutes. Following that, antibiotic discs were positioned in petri plate and incubated for 24 hours at 37p C[14]. The tested antibiotics like Ampicillin (2mcg), Ceftriaxone (30mcg), Levofloxacin (5mcg), Tazobactam (10mcg), Gentamycin (10mcg), Meropenem (10mcg), Imipenem (10mcg), Co-trimoxazole (25mcg), Tobramycin (30mcg), Norfloxacin (10mcg), Methicillin (10mcg), Azithromycin (15mcg), Ceftazidime (30mcg), Cefoxitin (30mcg), Cefazolin (30mcg), Ciprofloxacin (5mcg), Ticarcillin-Calvunate (15mcg), Tetracycline (30mcg), Fosfomycin (200 mcg) from Himedia, Mumbai, were procured. Following a 24 h incubation, the diameter (mm) of the inhibition was measured using the meter ruler and recorded in accordance with CLSI[15]. Only one of the isolates is subsequently studied if two or even more isolates collected from the same sample site showed identical results.

Determination of antibiotic resistance and multidrug resistance pattern

The Multi-Drug Resistant Bacteria (MDR) were those bacteria that have demonstrated resistance to more than 12 different antibiotics. The MAR index value for each bacterial isolate ~~is~~ was calculated based on the formula.

MAR Index Value = M/n

Where, M is the number of drugs/ antibiotics to which the bacterial isolate shows resistance; n is the total number of drugs/antibiotics employed[16]. Mostly, MAR index greater than 0.2 is an indication that the isolate is MDR[17].

Cultural and biochemical characterization of MDR isolates

MDR bacterial isolates obtained from MAR index were further characterized by both cultural and biochemical tests according to the Bergey's Manual of Systematic Bacteriology[18].

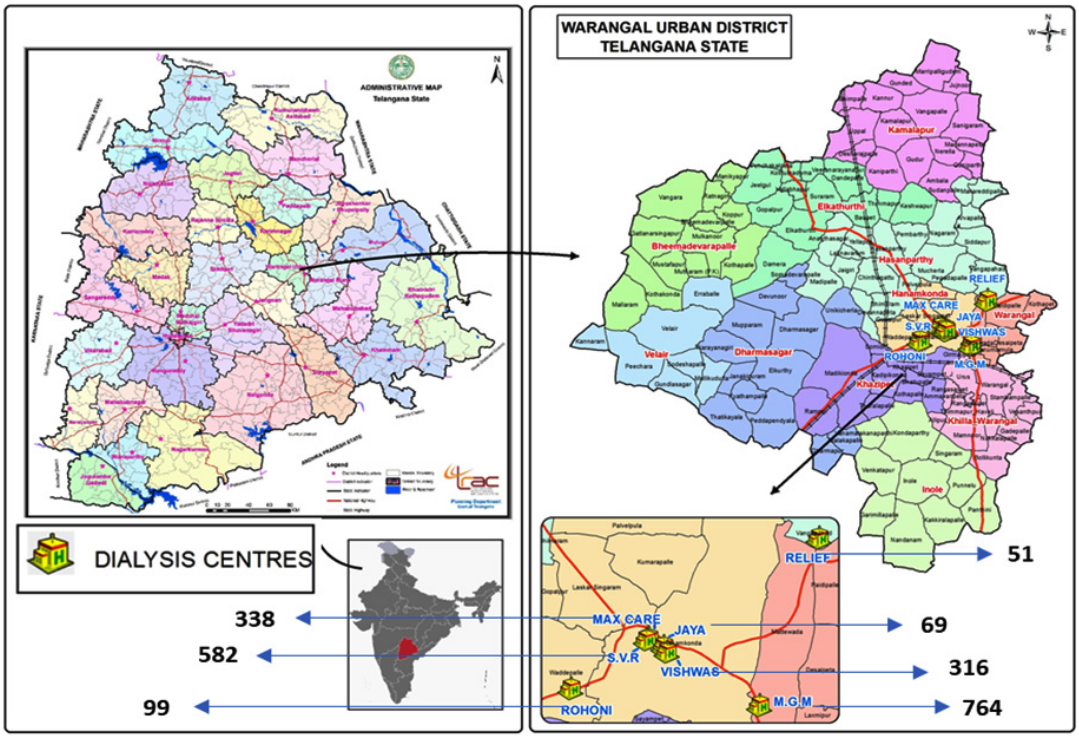


Fig. 1. Demographic details of the sample collection centres with positive cases

Cell morphology was microscopically observed using Gram staining. Biochemical characteristics viz., IMViC, oxidase, nitrate reductase, H_2S production, sugar fermentation, catalase, amylase and gelatin hydrolysis, etc. were carried out[19].

Molecular identification of MDR isolates

DNA isolation and PCR amplification

DNA from 24 h old bacterial isolates was extracted using phenol-chloroform and stored at 16p C[20]. Using a set of forward primer, 27F (50'-AGAGTTTGATCCTGGTCAG-3') and reverse primer, 1492 R, the 16S rRNA genes were amplified (5'- GGTTACCTTGTTACGACTT-3') After PCR amplification, DNA was purified by QIAGEN QIAquick PCR Purification kit (Cat. No./ID:28104) and 15 ml of the amplicons were electrophoresed on 1% agarose gel for 1hr at 80 Volts. The DNA bands were then visualized under a UV-transilluminator and the purified product was sent for sequencing[21].

16S rRNA gene sequencing and phylogenetical analysis

The sequencing of 16S rRNA gene of the bacterial isolates was performed by Sanger's

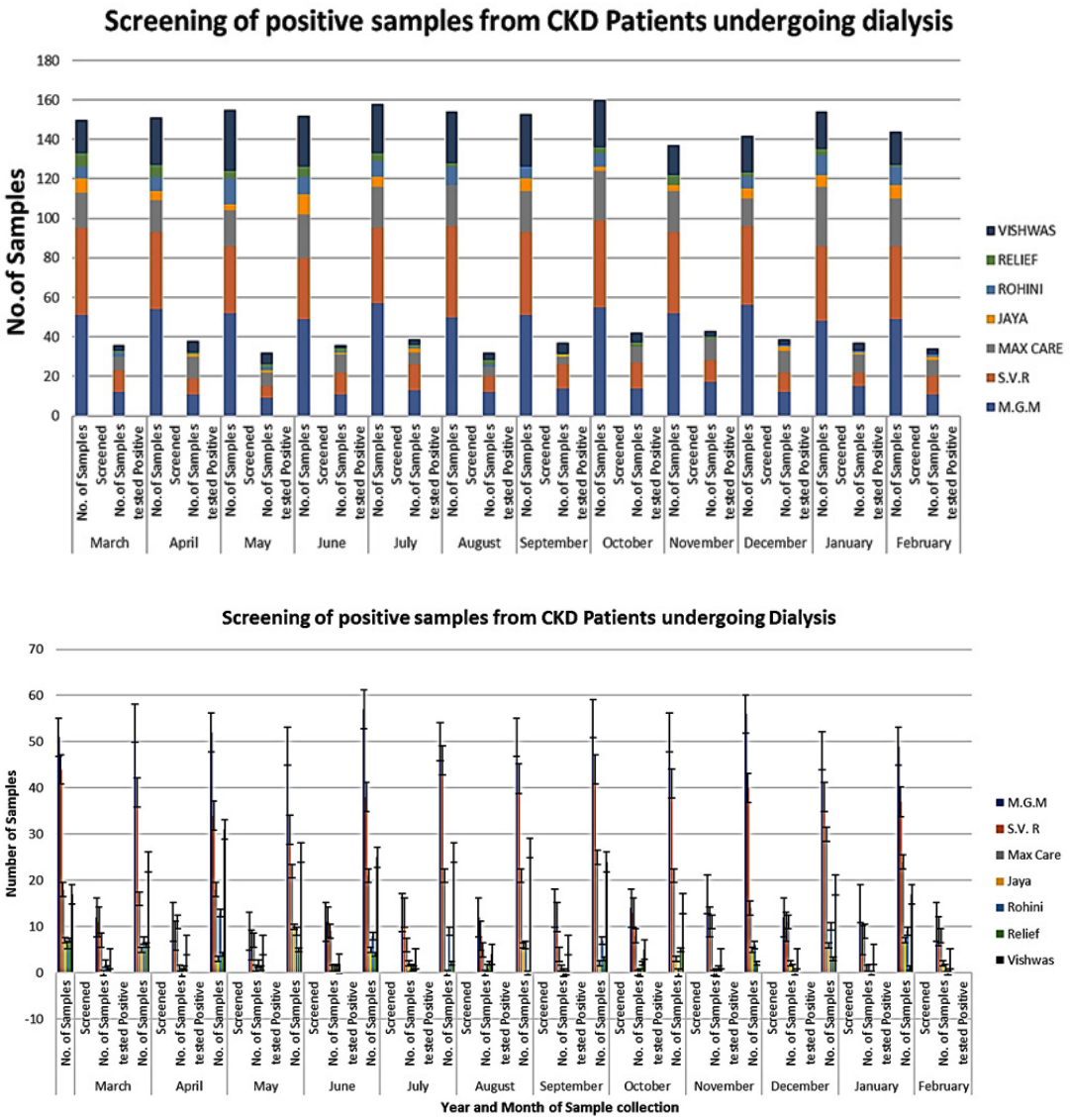


Fig. 2. Screening of positive samples from CKD patients undergoing dialysis

Table 1. Screening of positive urine samples for Bacteria from CKD Patients undergoing Dialysis

Name of Hospital		M.G.M	S.V. R	Max Care	Jaya	Rohini	Relief	Vishwas
March	No. of SamplesScreened	51	44	18	7	6	7	17
	No. of Samplestested Positive	12	11	7	0	2	1	3
April	No. of SamplesScreened	54	39	16	5	7	6	24
	No. of Samplestested Positive	11	8	11	1	0	1	6
May	No. of SamplesScreened	52	34	18	3	13	4	31
	No. of Samplestested Positive	9	6	7	1	2	1	6
June	No. of SamplesScreened	49	31	22	10	9	5	26
	No. of Samplestested Positive	11	11	9	1	1	1	2
July	No. of SamplesScreened	57	38	21	5	8	4	25
	No. of Samplestested Positive	13	13	6	2	1	1	3
August	No. of SamplesScreened	50	46	21	0	9	2	26
	No. of Samplestested Positive	12	8	5	0	1	2	4
September	No. of SamplesScreened	51	42	21	6	6	0	27
	No. of Samplestested Positive	14	12	4	1	0	0	6
October	No. of SamplesScreened	55	44	25	2	7	3	24
	No. of Samplestested Positive	14	13	8	0	0	2	5
November	No. of SamplesScreened	52	41	21	3	0	5	15
	No. of Samplestested Positive	17	11	11	0	0	1	3
December	No. of SamplesScreened	56	40	14	5	6	2	19
	No. of Samplestested Positive	12	10	11	2	1	0	3
January	No. of SamplesScreened	48	38	30	6	10	3	19
	No. of Samplestested Positive	15	7	9	1	1	0	4
February	No. of SamplesScreened	49	37	24	7	9	1	17
	No. of Samplestested Positive	11	9	8	2	1	0	3
Total samples Screened(N)		764	582	338	69	99	51	316
No. of Positive Samples(n)		151	119	96	11	10	10	48
Cumulative Number of Samples (N)		2219						
Total No. of Samples Tested Positive for AMR		445 (20.05 %)						
Total No. of Samples Tested negative for AMR		1774 (79.94 %)						

method using Applied Biosystems 3730xL analyser by Barcode Biosciences, Bangalore India. Using the BLAST programme, the FASTA sequences were further analysed for taxonomical identification by comparing them to a database of 16S rRNA sequences from NCBI[22]. With the use of the NJ (Neighborhood Joining) method, a phylogenetic tree was generated for the alignments of the eight closely related matches with the query sequences[23].

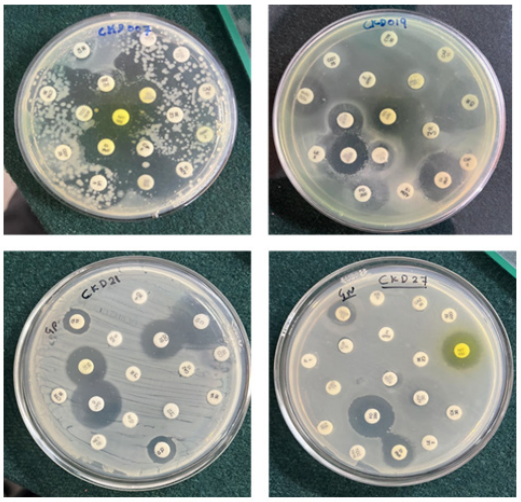


Fig. 3. Disc diffusion antibiotic testing of isolates

RESULTS AND DISCUSSION

Initially, the urine samples were assessed for the amount of serum creatinine and eGFR and a different pattern was noted in the first positive culture, according to different eGFR categories. Gram positive MDR bacteria increased while Gram negative MDR bacteria decreased from eGFR between 60–104 ml/min/1.73 m^2. *Enterococcus sp*., were the predominant MDR bacteria, followed by *Escherichia* sp., *Klebsiella* sp., *Enterobacter* sp., and *Providencia* sp. Compared with eGFR between 60 -104 ml/min/1.73 m^2, the proportion of *E. coli* started to rise as the eGFR declined.

The crude MDR ratio increased with decreasing eGFR for *E. coli, Klebsiella,*

Table 2. Antibiogram and MAR Index of MDR bacterial Isolates

Antibiotic Tested		Bacterial isolate				
Class of Antibiotics	Antibiotic (mcg)	CKD_07_1	CKD_19	CKD_21	CKD_27_1	CKD_31_1
Ampicillin	Ampicillin-2	R	S	S	R	R
Macrolide	Azithromycin-10	S	R	R	R	R
Cephalosporins	Ceftriaxone-30	R	R	S	R	R
	Cephalexin-20	S	R	R	S	S
	Ceftazidime-30	R	R	R	R	R
	Cefoxitin-30	R	R	S	R	R
	Cefazolin-30	R	S	R	R	R
Quinoline	Norfloxacin-10	S	R	R	R	S
Fluoroquinolone	Levofloxacin-5	R	R	R	R	R
	Ciprofloxacin-5	R	R	S	S	R
Beta-lactam	Tazobactam-10	R	R	R	S	S
	Ticarcillin-Calvunate-15/10	R	S	S	R	R
	Methicillin-10	R	S	S	R	S
Aminoglycoside	Gentamycin-10	R	S	R	S	R
	Tobramycin-30	R	R	R	S	R
Carbapenem	Meropenem-10	S	S	S	R	R
	Imipenem-10	S	S	R	S	R
Tetracycline	Tetracycline-30	S	R	S	R	S
Sulphonamide	Co-trimoxazole-25	R	R	R	R	R
Fosfomycin	Fosfomycin-200	S	R	R	S	S
	MAR Index	0.7	0.35	0.4	0.35	0.3

S = Sensitive; R = Resistant

Enterobacter sp., Enterococcus sp., but decreased for *Providencia sp.* These results are in relation with the studies conducted by Evans and his coworkers[24]. Also, in a study by two different research teams lead by James and Dalrymple, it was found that eGFR e" 105 ml/min/1.73 m^2 might indicate malnutrition, which would be predisposed to high risk of infection[12,25].

The results from various hospitals over the course of a year indicate varying numbers of samples screened and tested positive for antimicrobial resistance (AMR). Hospital M.G.M screened 764 samples, with 151 testing positive for AMR. Similarly, S.V.R screened 582 samples, of which 119 were positive. Max Care screened 338 samples, yielding 96 positive cases. Hospital Jaya had 11 positive results out of 69 samples. Hospital Rohini, Relief, and Vishwas recorded 10, 10, and 48 positive cases out of 99, 51, and 316 screened samples respectively. In total, 445 samples (20.05%) tested positive for AMR, while 1774 samples (79.94%) tested negative, culminating in a cumulative screening of 2219 samples (**Table 1, Figure 2**).

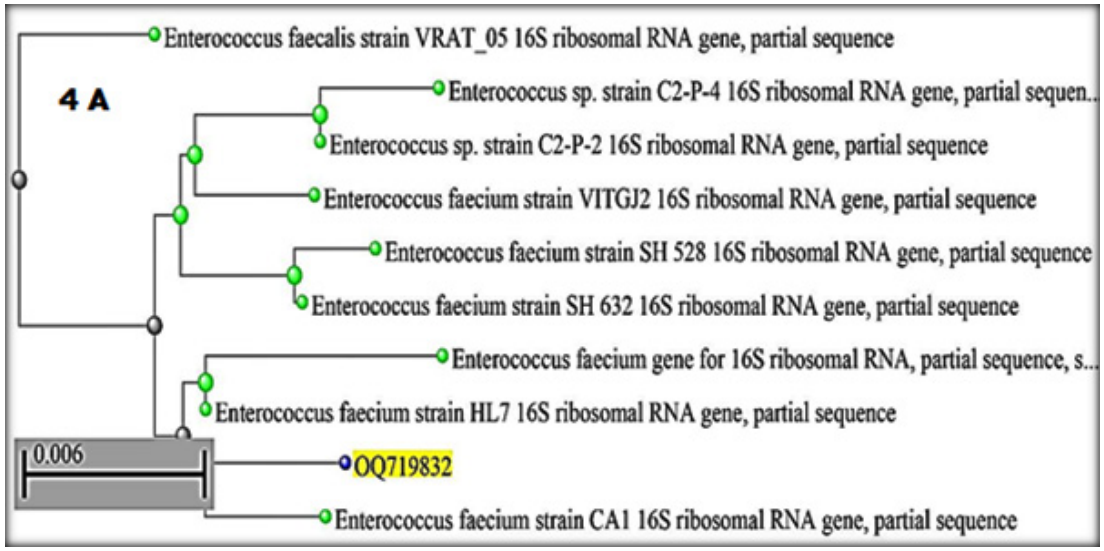
Table 3. Morphological and biochemical characterization of MDR bacterial isolates

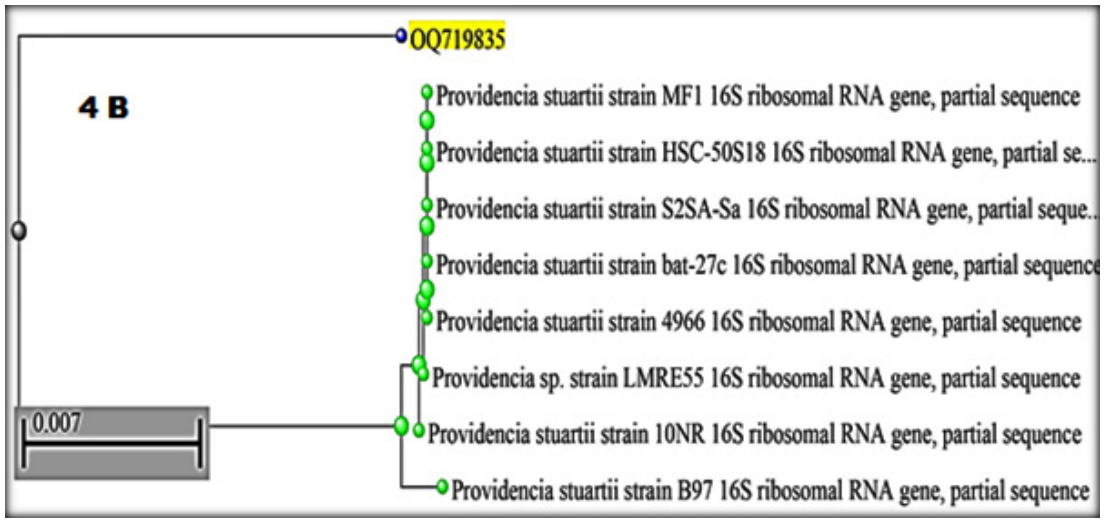
Morphological and biochemical test	Name of the MDR bacterial isolate				
	CKD_07_1	CKD_19	CKD_21	CKD_27_1	CKD_31_1
Gram stain	+	-	-	-	-
Motility	-	+	-	+	+
Catalase production	-	+	+	+	+
Gelatin hydrolysis	-	-	-	-	-
Voges Proskauer	+	-	+	+	-
Lipase	-	-	-	-	-
Methyl red	-	+	-	-	+
Oxidase	+	-	-	-	-
Indole production	+	+	-	-	+
Citrate	-	+	+	+	-
Urea hydrolysis	-	+	+	-	-
Nitrate reduction	-	+	+	+	+
D-Glucose (acid/gas)	-/+	+/-	-/+	+/+	+/+
Lactose	+	-	+	-	+
Sucrose	+/-	+/-	+	+	+/-
L-Arabinose	+	-	+	+	+
Glycerol	+	-	+	+	-
D-Glucoside	-	-	+/-	+	-
Raffinose	-	-	+	+	+/-
D-Sorbitol	-	-	+	+	+
D-Mannitol	+	-	+	+	+
Maltose	+	-	+	+	+
D-Adonitol	-	-	+	-	-
Cellobiose	+	-	+	+	-

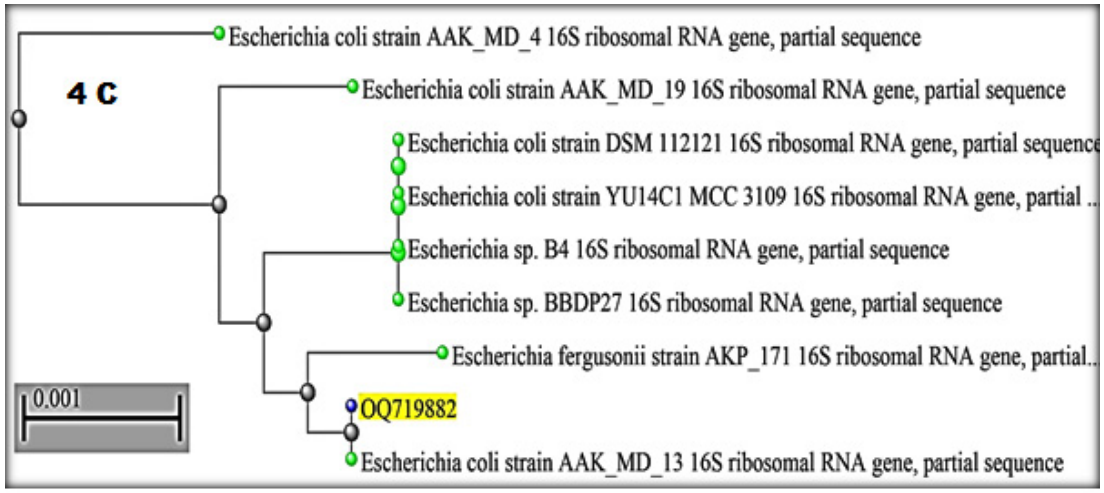
Table 4. MDR bacterial isolates and their accession numbers

Name of the Isolate	Accession Number
CKD_07_1	OQ719832
CKD_19	OQ719835
CKD_21	OQ719895
CKD_27_1	OQ719944
CKD_31_1	OQ719882

36 colonies with unique morphology were picked up and tested for antibiotic sensitivity or resistance. The Multi Antibiotic Resistance (MAR) index is an indication of the bacterial isolates showing resistance to different antibiotics. If the MAR index value is more than 0.2 (>0.2), the bacteria is considered as multi-drug-resistant bacteria. From the MAR indices, it was found that 5 out of 36 isolates exhibited resistance to multiple antibiotics (**Figure 3, Table 2**).


4 A
Enterococcus faecalis strain VRAT_05 16S ribosomal RNA gene, partial sequence
Enterococcus sp. strain C2-P-4 16S ribosomal RNA gene, partial sequen...
Enterococcus sp. strain C2-P-2 16S ribosomal RNA gene, partial sequence
Enterococcus faecium strain VITGJ2 16S ribosomal RNA gene, partial sequence
Enterococcus faecium strain SH 528 16S ribosomal RNA gene, partial sequence
Enterococcus faecium strain SH 632 16S ribosomal RNA gene, partial sequence
Enterococcus faecium gene for 16S ribosomal RNA, partial sequence, s...
Enterococcus faecium strain HL7 16S ribosomal RNA gene, partial sequence
0.006
OQ719832
Enterococcus faecium strain CA1 16S ribosomal RNA gene, partial sequence


OQ719835
4 B
Providencia stuartii strain MF1 16S ribosomal RNA gene, partial sequence
Providencia stuartii strain HSC-50S18 16S ribosomal RNA gene, partial se...
Providencia stuartii strain S2SA-Sa 16S ribosomal RNA gene, partial seque...
Providencia stuartii strain bat-27c 16S ribosomal RNA gene, partial sequence
Providencia stuartii strain 4966 16S ribosomal RNA gene, partial sequence
Providencia sp. strain LMRE55 16S ribosomal RNA gene, partial sequence
0.007
Providencia stuartii strain 10NR 16S ribosomal RNA gene, partial sequence
Providencia stuartii strain B97 16S ribosomal RNA gene, partial sequence


Escherichia coli strain AAK_MD_4 16S ribosomal RNA gene, partial sequence
4 C
Escherichia coli strain AAK_MD_19 16S ribosomal RNA gene, partial sequence
Escherichia coli strain DSM 112121 16S ribosomal RNA gene, partial sequence
Escherichia coli strain YU14C1 MCC 3109 16S ribosomal RNA gene, partial ...
Escherichia sp. B4 16S ribosomal RNA gene, partial sequence
Escherichia sp. BBDP27 16S ribosomal RNA gene, partial sequence
Escherichia fergusonii strain AKP_171 16S ribosomal RNA gene, partial...
0.001
OQ719882
Escherichia coli strain AAK_MD_13 16S ribosomal RNA gene, partial sequence

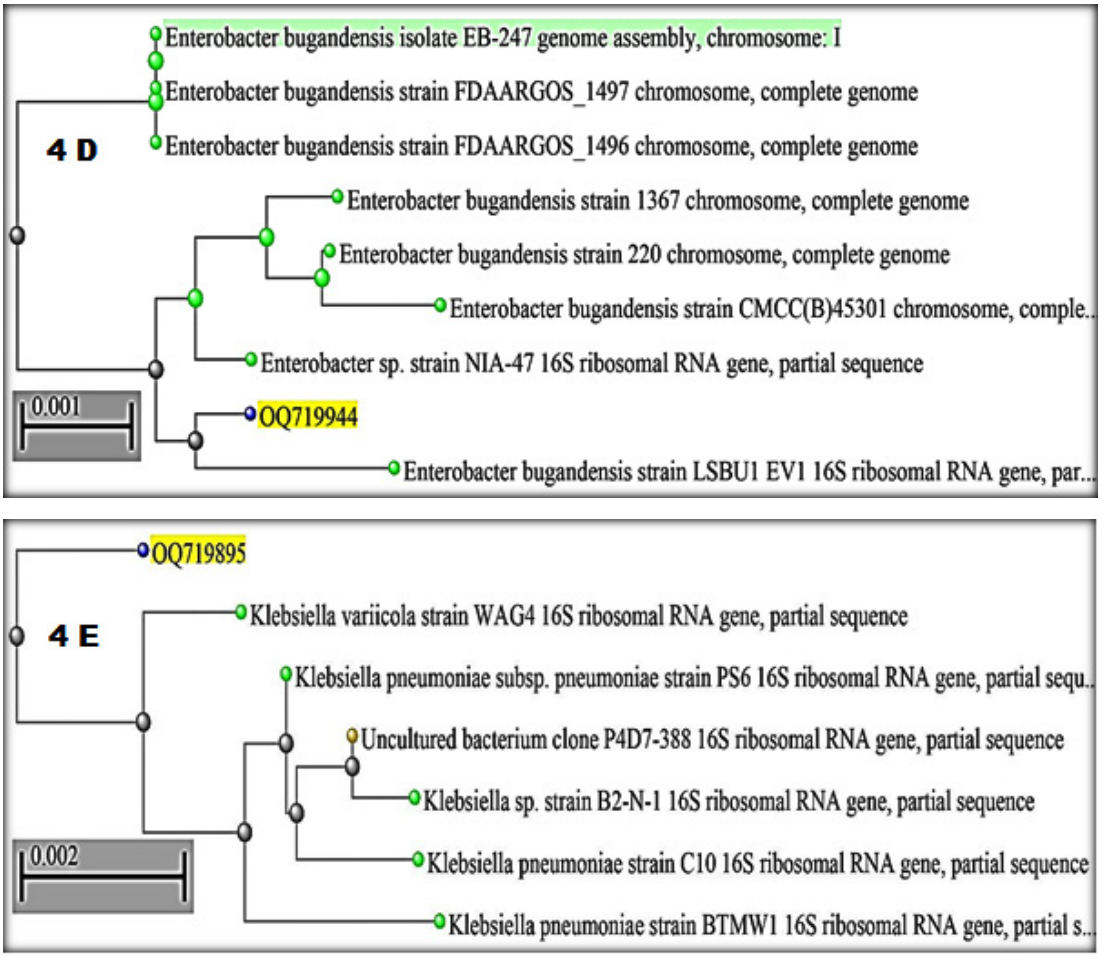


Fig. 4. Phylogenetic tree of (4.A) CKD_7_1 (4.B) CKD_19 (4.C) CKD_31_1 (4.D) CKD_27_1 (4.E) CKD_21

Isolates viz., CKD_7_1, CKD_19, CKD_21, CKD_27_1 and CKD_31 was found to be resistant to most of the antibiotics. Almost all isolated showed resistance towards Ceftazidime and Levofloxacin. Highest MAR index (0.7) was shown by CKD_07_1 and the least by CKD_31_1 (0.3). CKD_07_1 showed resistance to all the antibiotics except Azithromycin, Norfloxacin, Meropenem, Imipenem, Tetracycline, Cephalexin and Fosfomycin; CKD_19 was found to be sensitive to the Ampicillin, cefazolin, Ticarcillin, Methicillin Gentamycin, Meropenem and imipenem. From the results tabulated in table 2, it is evident that patients with CKD are possibly more likely to have a resistant strain.

In a study conducted by Moges and his co-workers, multidrug resistance was also prevalent in Gram-negative bacteria like *E. coli*, *Enterobacter* sp. *Citrobacter* sp. and *Klebsiella* sp. and Gram-positive bacteria like *Staphylococcus* sp. which is in accordance with our study[26].

Research efforts have extensively delved into the antibiotic sensitivity profiles of *Enterococcus faecalis*. Numerous investigations have explored the susceptibility of *Enterococcus faecalis* to various antibiotics. In a recent study conducted by Khalil et al. (2022), the findings highlighted that a majority of *E. faecalis* strains exhibited resistance to tetracycline, erythromycin, levofloxacin, and quinupristin-dalfopristin[27]. In parallel, Samani et al. (2021) conducted another study focused on the prevalence of virulence genes and the antibiotic resistance pattern of *Enterococcus faecalis* isolated from urinary tract

infections in Shahrekord, Iran and found that it was resistant to Norfloxacin, Vancomycin, tetracycline, ciprofloxacin and erythromycin[28]. This is in complete contradiction to the isolate (CKD_7_01) in our study which was sensitive to Norfloxacin and tetracycline.

Providencia stuartii, in a study conducted by Stock and Wiedemann (1998), showed resistance to polymyxin *B, colistin* and nitrofurantoin, some aminoglycosides and Penicillins, older cephalosporins, tetracyclines, gentamicin, tobramycin and chloramphenicol[29]. The results were of our isolate (CKD_19) in accordance to the literature.

CKD_21 also showed resistance to many antibiotics similar to a study conducted by Rodriguez et al. (2019), researchers analyzed the antibiotic susceptibility of *Klebsiella variicola* isolates. They found variable resistance rates to commonly used antibiotics, including ampicillin, amoxicillin/clavulanate, ciprofloxacin, and gentamicin[30]. Another study by Feng et al. (2020) investigated the genetic basis of antibiotic resistance in *Klebsiella variicola*. The research highlighted the presence of various resistance genes, including those conferring resistance to beta-lactams, aminoglycosides, and quinolones[31].

In a study by Urbaniak *et al* (2018), it was found that *E. bugandensis* displayed resistance to cefazolin, cefoxitin, erythromycin, oxacillin, penicillin, and rifampin. Additionally, concerning ciprofloxacin and gentamicin, the strains exhibited either resistance or intermediate resistance. Notably, with tobramycin, a combination of resistant, intermediate resistant, and susceptible strains was observed which was contradictory to our isolate (CKD_27_01) being sensitive to tobramycin[32].

In a study by McGregor et al. (2013), which investigated antibiotic resistance patterns of *Escherichia coli* urinary isolates from outpatients, it was found that *E. coli* demonstrated susceptibility to ampicillin, amoxicillin-clavulanate, ciprofloxacin, and nitrofurantoin[33]. The results are in contract with the finding of McGregor.

The MDR bacterial isolates were further analysed by morphological, biochemical and molecular analysis. Biochemical and cultural characteristics of all isolates CKD_7_1, CKD_19, CKD_21, CKD_27_1 and CKD_31_1 was studied and **Table 3** specifies the structural and biochemical characteristics of the isolated strains.

The DNA from all the isolated strains was isolated, amplified and the PCR amplicons were analysed for molecular identification by 16S rRNA sequencing ~~by~~ employing Sanger's method. Nucleotide BLAST studies revealed that the 16S rRNA sequences of the isolates, CKD_07_1 (919 bp), CKD_19 (711 bp), CKD_21 (705 bp), CKD_27_1 (875 bp), CKD_31_1 (897 bp) was found to be *Enterococcus faecium*, *Providencia stuartii*, *Klebsiella variicola*, *Enterobacter bugandensis* and *Escherichia coli* respectively when checked with nearest homology.

The partial sequences of 16s rRNA gene for the MDR isolates were submitted to the GenBank, NCBI and can be accessed under the given accession numbers (**Table 4**). The phylogenetic trees were constructed for few MDR bacterial isolates (**Figure 4**).

CKD appears to be a health risk for bacterial infection brought on by pathogens that are resistant to antibiotics, but the majority of published studies are concentrated on the risk of MDR bacterial infections in patients with end stage kidney disease (ESKD) who are receiving dialysis, and there are few studies that examine the association between early stages of CKD and antibiotic susceptibility[34].

CONCLUSIONS

The prevalence of antibiotic-resistant strains, including *Enterococcus faecium, Providencia stuartii, Klebsiella variicola, Enterobacter bugandensis*, and *Escherichia coli*, among CKD patients underscores the urgency of addressing antimicrobial resistance. On the other hand, Cephalosporins and the beta lactam class of antibiotics are frequently administered in case of any bacterial infections, which could be the reason for development of resistance in most of the bacteria. In order to prevent the overuse of antibiotics and shorten the treatment times, it is vital to develop efficient guidelines for the judicious usage of antibiotics for CKD patients. Research into plant extracts' efficacy against MDR bacteria is on-going, where they can also be used to combat multidrug resistant bacteria. By leveraging *in silico* methods and data analysis, we can identify

new drug targets and develop more effective antibiotics to combat MDR infections in CKD patients with UTIs also. Future challenges in this field include the need to improve the accuracy and reliability of *in silico* analysis, as well as to validate the findings of *in silico* studies with experimental data that can account for the complex and dynamic nature of multidrug resistance in CKD patients, including the impact of co-morbidities and drug interactions.

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Conflict of Interests

The authors declare that there are no conflicts of interest.

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