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# Trends and patterns of UTIs in Sindh, Pakistan with a focus on vancomycin-resistant enterococci

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**Abstract**: Urinary tract infections (UTIs) remain the most frequent clinical diagnosis and Vancomycin-resistant *Enterococci* (VRE) second-leading cause of UTIs. The aims of this study were to ascertain the patterns and prevalence of UTIs in Sindh and underlying resistance mechanisms for VRE. Bacterial colonies were identified traditionally from a total of 33272 urine samples. *Enterococcus* species were identified using Facklam and Collins scheme. Antibiotic susceptibility was determined by Kirby-Bauer method and minimum inhibitory concentration (MIC) by E-test. VRE phenotypes were checked using vancomycin and teicoplanin discs. UTIs prevalence during November-2022 to December-2023 is 22%. Reproductive-age women and elders affected most. Predominant Gram-negative pathogens were *Escherichia coli* (47.6%), *Klebsiella spp.* (15.7%), *Pseudomonas aeruginosa* (13.3%) and *Morganella morganii* (9.3%) while *Enterococci* were the leading Gram-positive pathogen (46%). *E. faecium* was the most prevalent (74.8%) followed by *E. faecalis* and motile *Enterococci.* VRE were noted 16.3%. All *Enterococci* were resistant to cefotaxime, ampicillin and co-amoxiclav and susceptible to linezolid. Each *E. faecium* was VanA phenotype while 20% *E. faecalis* were VanB phenotype. Vancomycin-resistance has increased by two-fold in Pakistan. The negligent-opportunistic *M. morganii* has emerged the fourth-leading cause of UTIs. We recommend focusing on VanRS system, a potential target of novel therapeutics for VRE.

**Keywords**: Antibiotic resistance; Prevalence; Phenotype; Urinary tract infections (UTIs); Vancomycin-resistant *enterococci* (VRE)

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## INTRODUCTION

Urinary tract infections (UTIs) are the most frequent reported clinical diagnosis in Pakistan in the last decade (Bilal *et al*., 2021). UTIs rank third after respiratory and gastro-intestinal tract infections in humans (Najar *et al*., 2009). Women suffer most due to their physiology of reproductive system and incidence are higher during pregnancy (Vasudevan, 2014). Although a range of uro-pathogens involved in UTIs, Gram-negative bacteria are predominantly encountered and Gram-positive bacteria contributes 15-20% (Bano *et al*., 2012). Generally UTIs are self-limiting but have a propensity to recur. A number of opportunistic nosocomial Gram positive pathogens causing serious infections such as endocarditis, septicemia and UTIs have emerged in past decades. The *Enterococcus* group is a dominant intestinal flora of human and animals. At present however, >40 species of *enterococci* have been reported, the most frequent for human infections are *E. faecalis* (80-90%) and *E. faecium* (10-15%). Motile *enterococcus* species *E. gallinarum* and *E. casseliflavus* rarely cause bacteremia, meningitis, endocarditis and UTIs (Khan and Pirzada, 2015).

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β-lactams, aminoglycosides, chloramphenicol, quinolones, tetracyclines, macrolides and streptogramins are the treatment of choices while glycopeptides especially vancomycin and teicoplanin are the reserved therapeutic options (Ullah *et al*., 2015). Multidrug-resistant enterococci exhibit intrinsic resistance to beta-lactams and aminoglycosides due to mutation or overproduction of penicillin binding protein and slow uptake of aminoglycosides (Tang *et al*., 2014). Acquired resistance is exhibited through transposons, plasmids or horizontal gene transfer against quinolones, tetracyclines, macrolides and streptogramins. Resistance to chloramphenicol is either enzymatic or plasmid-borne. Acquired resistance raise concerns about the transfer of vancomycin resistance genes to *Staphylococcus aureus* (Raza *et al*., 2018). Since the first report of VRE from England in 1988 (Raza *et al*., 2018) and from Pakistan in 2002 (Khan *et al*., 2002), the VRE has spread around the globe and narrowed therapeutic options. VRE are the leading cause of hospital-acquired bloodstream and UTIs. Prolonged hospitalization, age extremities, injudicious or prophylactic use of antibiotics, animal husbandry and hospital workers have been related to the high prevalence of VRE (Raza *et al*., 2018, Wada *et al*., 2021). Morbidity and mortality rates are higher for VRE infections.

Vancomycin blocks the cell wall formation by binding to the D-alanyl-D-alanine of the elongating peptidoglycan (Stogios and Savchenko, 2020). Although nine vancomycin resistance genes (VanA, VanB, VanC, VanD, VanE, VanG, VanL, VanM and VanN) have been identified for *enterococci* the VanA and VanB phenotypes are the most prevalent. The dominant phenotype VanA confers resistance to both vancomycin and teicoplanin while VanB phenotype is inducibly resistant to vancomycin and shows susceptibilty towards teicoplanin (Raza *et al*., 2018). The VanA gene cluster is encoded by a transposon (Tn1546) located on a plasmid and does not confer resistance alone (Selim, 2022). The VanA gene cluster in association with other genes: VanH, VanR, VanS, VanX, VanY and VanZ located on Tn1549 regulate, express and synthesize the abnormal peptidoglycan precursors D-alanyl-D-Lac and D-alanyl-D-Ser to which vancomycin binds with low affinity (Selim, 2022). VanS detects vancomycin and in turn activates VanR which regulates the expression of vancomycin-resistance genes. The VanB gene cluster is encoded by Tn1547 and is located on chromosome or plasmid. The genes of VanB cluster are VanHB, VanRB, VanSB, VanXB and VanYB. The VanB isolates are susceptible to teicoplanin and resistant to vancomycin, as VanRB-VanSB system is not triggered by teicoplanin. Treatment options for VRE include linezolid, daptomycin, tigecycline, fosfomycin and nitrofurantoin (Raza *et al*., 2018).

Urgent call of novel therapies for VRE by World Health Organization (WHO) (Selim, 2022) emphasizes on the current estimates of VRE infections and understanding of complex vancomycin resistance mechanisms . The aims of the study was to determine the patterns and trends of UTIs from 2022 to 2023 in Pakistan with a focus on prevalence and underlying resistance mechanisms for VRE.

## MATERIALS AND METHODS

### *Study duration and area*

This retrospective, cross-sectional study was conducted in three microbiology laboratories from November-2022 to December-2023. Inpatients and outpatients of both genders and all age groups with overt symptoms of UTIs were included in the study.

### *Specimen collection*

Midstream urine samples were obtained by clean-catch method in a wide-mouth sterile container. Samples were immediately transported to microbiology laboratories for culture evaluation.

### *Urine culturing and evaluation*

A total of 33272 urine samples from hospitalized and outpatients of both gender and all age groups were inoculated with calibrated (1ul) disposable wire loops on CLED agar by streak-plate method for isolated colonies. CLED agar plates were incubated aerobically for 18-48 hours at 37°C. Specimens showing bacterial growth $\geq 10^4$ CFU/ml were considered significant and processed further.

### *Morphological and biochemical identification*

Bacterial colonies were traditionally identified using colony morphology, microscopy, Gram's staining, motility, $H_2S$ production, catalase, coagulase and oxidase tests. Gram negative bacteria were conventionally identified using citrate utilization, triple sugar iron, urease and indole production. For *Enterococci,* single-type isolated colonies from CLED agar were inoculated in bile esculin agar, 6.5% NaCl, growth at 10 ℃ and 45 ℃ and survival at 60 ℃ for 30 minutes (Sherman, 1937). Final confirmation was performed using ABIS (Advanced Bacterial Identification Software) online (http://www.tgw1916.net/bacteria_logare.html). *Enterococcus* species identification was done according to the scheme of Facklam and Collins (Facklam and Collins, 1989).

### *Antimicrobial sensitivity testing (AST)*

Confirmed *Enterococci* were checked for the antibiotic susceptibility as per Clinical laboratory standard institute (CLSI) and European committee on antimicrobial susceptibility testing (EUCAST) guidelines (Gaur *et al*., 2023). The Kirby-Bauer disk diffusion method on Mueller Hinton agar was used for common antibiotics for the treatment of UTIs *i.e.* Ampicillin, Co-amoxicalv, Cefotaxime, Nitrofurantoin, Fosfomycin, Vancomycin, Teicoplanin, Ciprofloxacin, and Linezolid (Oxoid, UK). For vancomycin, a zone of inhibition $\leq$14 mm indicated resistance, 15-16 mm as intermediate and $\geq$17 mm as sensitive (Khandelwal *et al*., 2020). Vancomycin-resistance was further confirmed by MIC using E-test (bioMerieux, France).

### *Vancomycin resistance phenotypes*

VRE isolates exhibiting resistance to both vancomycin and teicoplanin were designated as VanA phenotypes while resistant to vancomycin and susceptible to teicoplanin were considered as VanB phenotypes (Raza *et al*., 2018).

### *Statistical analysis*

Data was stored and analyzed using MS Excel version 2010. The p-values were calculated using Chi-square formula and values < 0.05 were considered significant. All data generated or analyzed during this study are included in this published article

## RESULTS

A total of 33272 urine culture specimens were collected during November-2022 to December-2023. These specimens included 68% (n=22625) from outpatients and 32% (n=10647) from hospitalized patients.

The mean age of study population was 35.59 ± 10.95 years (range 08– 55 years). Of total specimens 22% (n=7320) were positive for bacterial pure culture, consisting of 56%

(n=4099) from outdoor patients and 44% (n=3221) from hospitalized patients, remaining were mixed bacterial growth (MBG) 8% (n=2662), insignificant bacterial growth (IBG) 5% (n=1664) and no growth (NG) 65% (n=21627) Fig. 1.

These positive pure bacterial cultures were mainly isolated from females 68% (n=4977) and a significant proportion of the samples showed bacteriuria 40% (n= 2928) and pyuria 86% (n=6295) while proteinuria was detected among 12% (n=878) of the specimens (Fig. 2).

Predominant number of females with positive urine cultures were in reproductive age group 69.4% (n=3459) (95% CI; 65.8-73.6; p< 0.001) while the frequency of positive urine culture was higher among males above 50 years of age 44.9% (n=1054) (95% CI; 41.8-47.7; p< 0.001) fig. 3.

In this study Gram-negative bacteria (GNR) 73% (n=5338) were found predominant cause of UTIs compared to Gram positive bacteria 27.07% (n=1982). Common GNR isolated were *Escherichia coli* 47.60% (n=2541), *Klebsiella spp.* 15.79% (n=843), *Pseudomonas aeruginosa* 13.30% (n=710), *Morganella morganii* 9.32% (n=498), *Proteus spp.*7.38% (n=394), *Acinetobacter baumannii* 4.10% (n=219), *Stenotrophomonas spp.* 1.16% (n=62), *Burkhuldaria spp.* 0.78% (n=42) *and* Typhoid *Salmonella* 0.54% (n=29), while common Gram positive bacteria isolated were *Enterococci* 46% (n=924), coagulase negative *Staphylococcus aureus* (CoNS) 25% (n=498), coagulase positive *Staphylococcus aureus* 22% (n=440), Group D *Streptococci* 3.4 % (n=68) and other *Streptococcal* species 2.6% (n=52). *E. faecium* 74.89% (n=692) and *E. faecalis* 18.61% (n=172) were the predominantly isolated *Enterococci* while *E. gallinarum* 4.54% (n=42) and *E. casseliflavus* 1.94% (n=18) were less frequently isolated (Fig. 4). Antimicrobial sensitivity testing (AST) of 924 *Enterococci* showed 16.39% (n=151) isolates were resistant to vancomycin (VRE). Predominant number of VRE were isolated from admitted patients 74% (n=112) (95% CI; 77.8-71.6; p < 0.001) while 26% (n=39) (95% CI; 24.2-27.9; p < 0.001) were recovered from outpatients. This finding highlights the wide spread of highly resistant variants of *Enterococci* among admitted patients and hospital settings and warns the physicians regarding injudicious use of antibiotics. Although, there was no significant difference of gender distribution among males (49.6%) and females (51.4%) (p > 0.05) for VRE very high level of resistance was determined against other antibiotics *i.e.* ciprofloxacin 82%, nitrofurantoin 40.39% and fosfomycin 32.45%. All *Enterococci* isolates were resistant to cefotaxime, ampicillin and co-amoxiclav, while all isolates were sensitive to linezolid (Fig. 5). This finding questions the use of β-lactams especially penicillins and cephalosporins for the treatment of UTIs caused by *Enterococci.* In this study, all of the VRE were either *E. faecium* or *E. faecalis*. None of the *E. gallinarum* or *E. casseliflavus* were found resistant to vancomycin. Although we found no significant difference of vancomycin resistance rate (p > 0.05) among *E. faecium* isolates (121/692, 17.4%) compared to *E. faecalis* (30/172, 17.4%), phenotypic classification revealed all vancomycin resistant *E. faecium* isolates were resistant to teicoplanin (100%) indicating the presence of *vanA* gene alone or both *vanA* gene and *vanB* gene while 20% (06/30) *E. faecalis* isolates were only resistant to vancomycin and were susceptible to teicoplanin indicating the presence of only *vanB* gene.

## DISCUSSION

In this study, two-years prevalence of UTIs was 22% during November-2022 to December-2023 (44% from hospitalized patients and 68% from females). This prevalence is much higher compared to a study during 2015-2019 which reported urinary infections rate 5.8% (Schmiemann *et al*., 2022). Another study reported the prevalence of UTIs 14.5% (Silva *et al*., 2022). In contrast a study from Bangladesh reported a very high prevalence (55%) of UTIs (Biswas *et al*., 2014). Comparing to a previous study from Karachi which recorded urinary infections rate 22% we hypothesize that UTIs are consistently high and in a state of equilibrium in our population. Our results are also in favor of previous studies which reported urinary infections occur more frequently in females (Schmiemann *et al*., 2022, Silva *et al*., 2022). Majority of the positive urine cultures were isolated from females of reproductive age and from males above 50 years of age in this study which agrees to a previous study that reported UTIs affect more elderly patients (Silva *et al*., 2022).

In this study a significant proportion of the urine samples showed bacteriuria 40% and pyuria 86% while proteinuria was detected among 12% of the specimens. Although pyuria inadequately predict bacteriuria the optimal cutoff point has been suggested 25 pus cells/hpf (Cheng *et al*., 2022). According to American Academy of Pediatrics (AAP), the definition of UTIs include both pyuria and bacteriuria but it has been estimated almost 10% of children lack pyuria with a positive urine culture (Nadeem *et al*., 2021) and sterile pyuria occurs in chronic kidney disease (CKD) (Kwon *et al*., 2020). In this study we did not correlate pyuria or proteinuria with bacteriuria. Like many prior investigations, GNR were the predominant cause of UTIs in this study. The top four GNR were *E. coli*, *Klebsiella spp.*, *P. aeruginosa* and *M. morganii* while *enterococci* were estimated the leading Gram positive bacteria in this research. Our findings agree with earlier information. In one study the most prevalent cause of UTIs was *E.coli* followed by *enterococci* (Biswas *et al*., 2014) whereas other studies report *E. coli* the most frequent uropathogen followed by *Klebsiella pneumoniae* (Hussain *et al*., 2020, Silva *et al*., 2022).

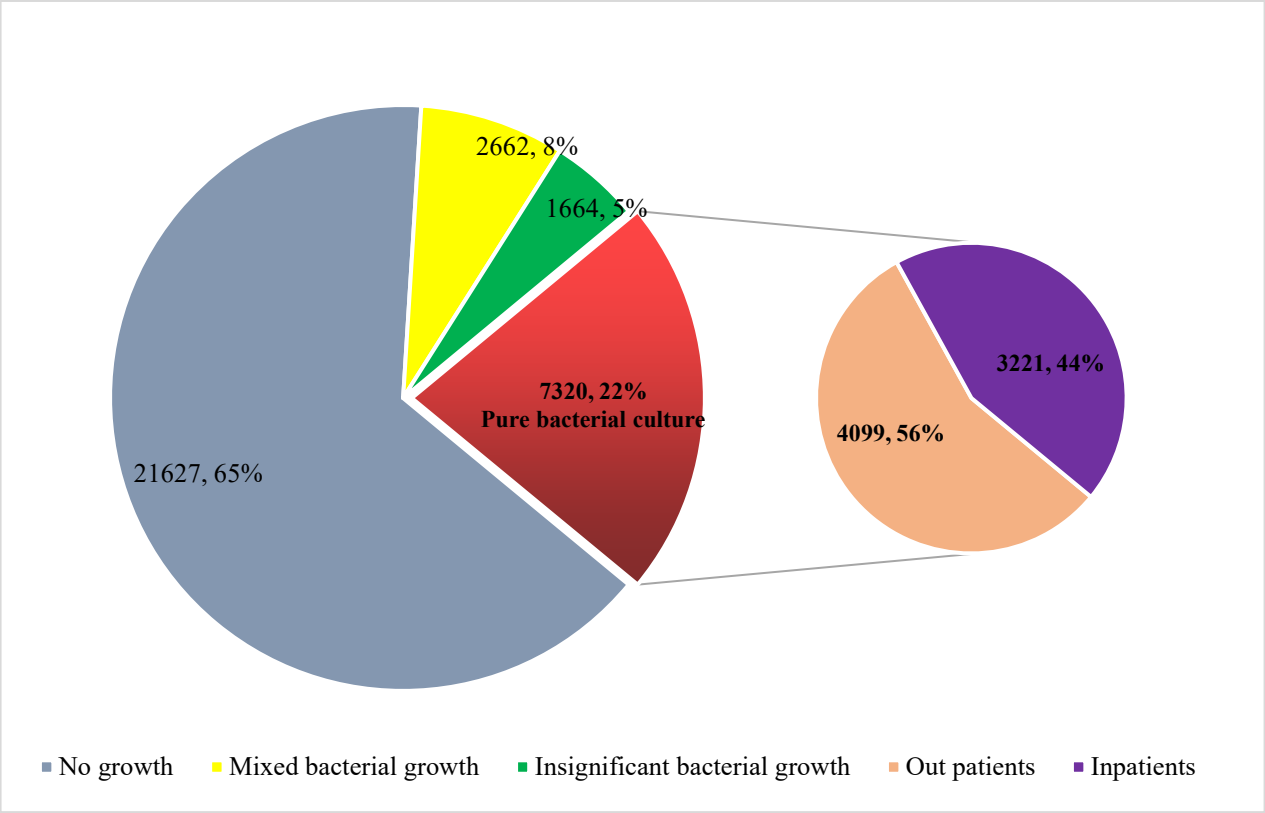


**Fig. 1**: Frequency of positive bacterial cultures in urine

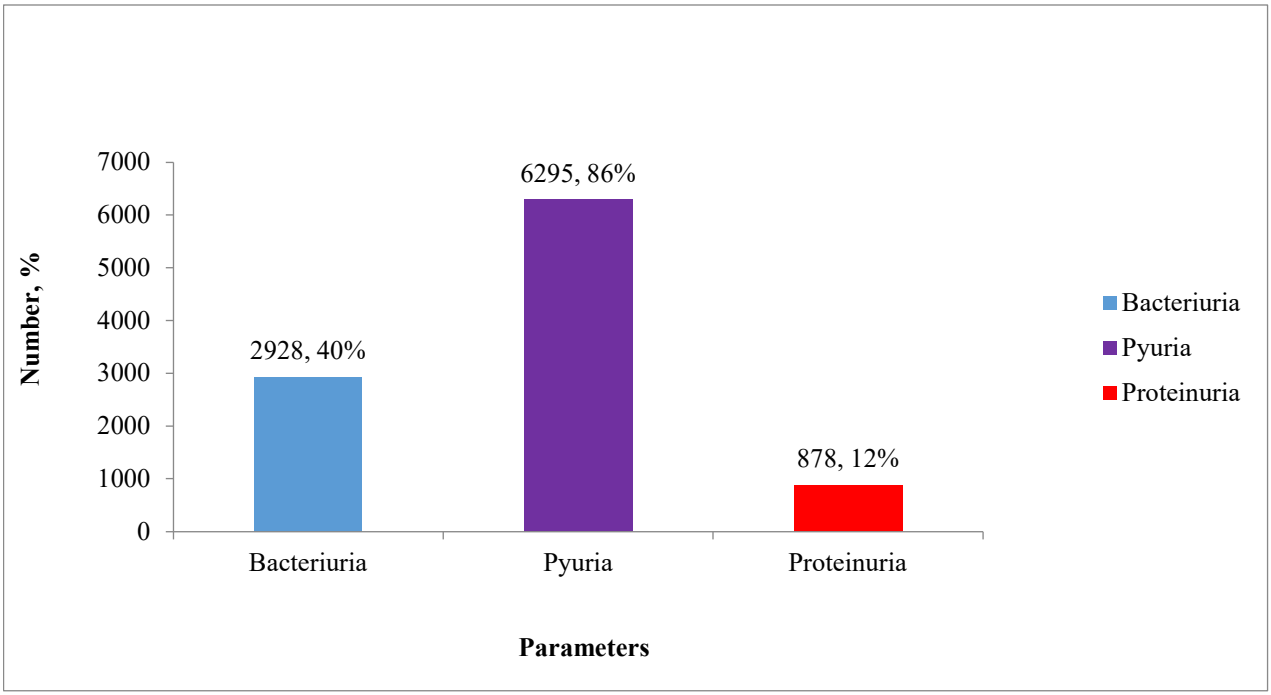


**Fig. 2**: Prevalence of different complaints with positive urine cultures

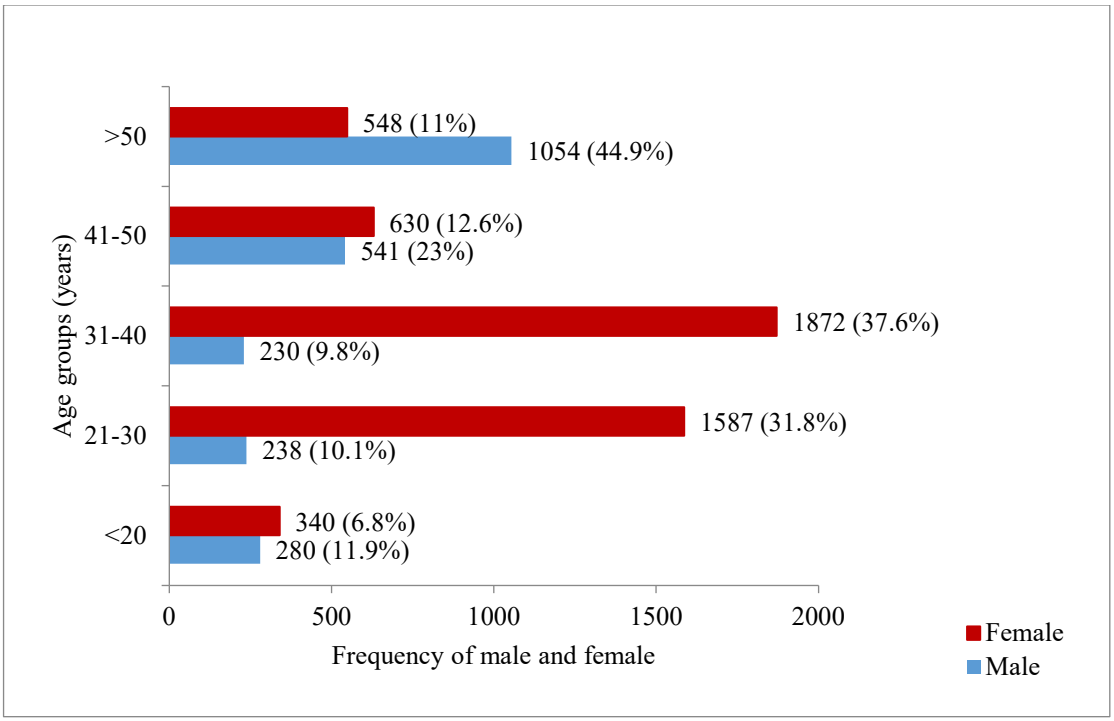


**Fig. 3**: Age distribution of patients according to gender with UTIs

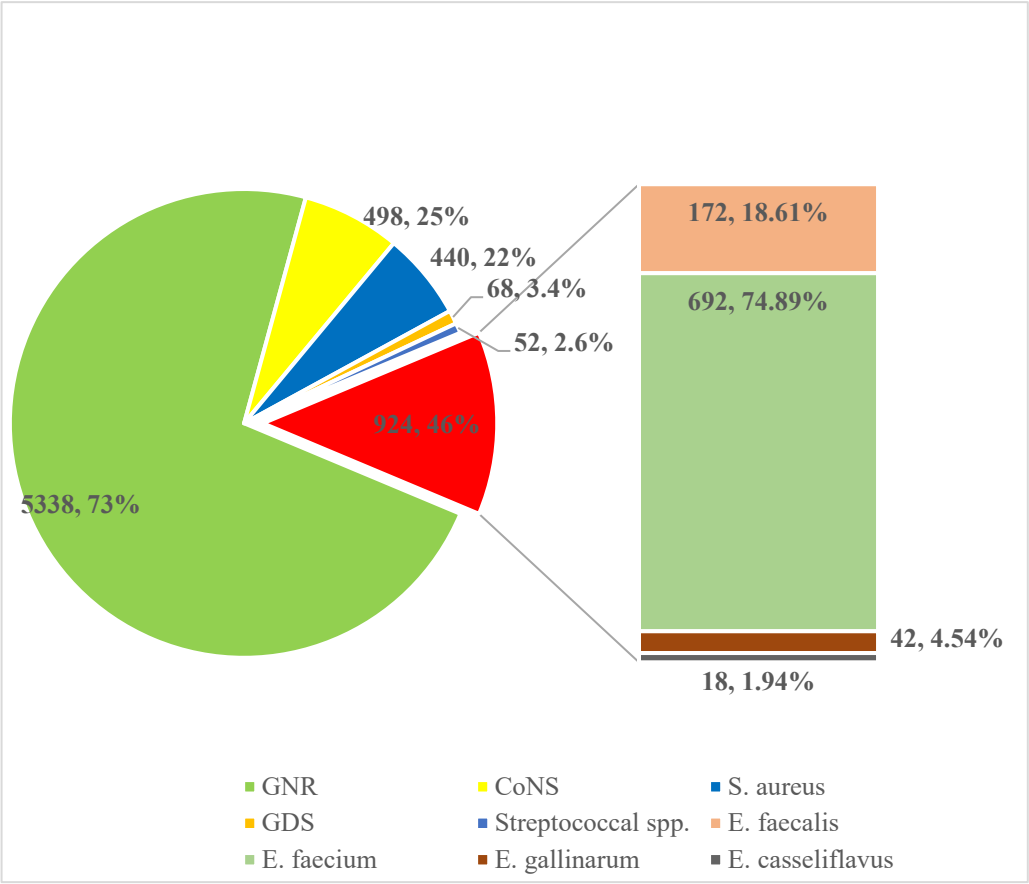


**Fig. 4**: Frequency of Gram negative and different Gram positive bacteria and *enterococci* in UTIs

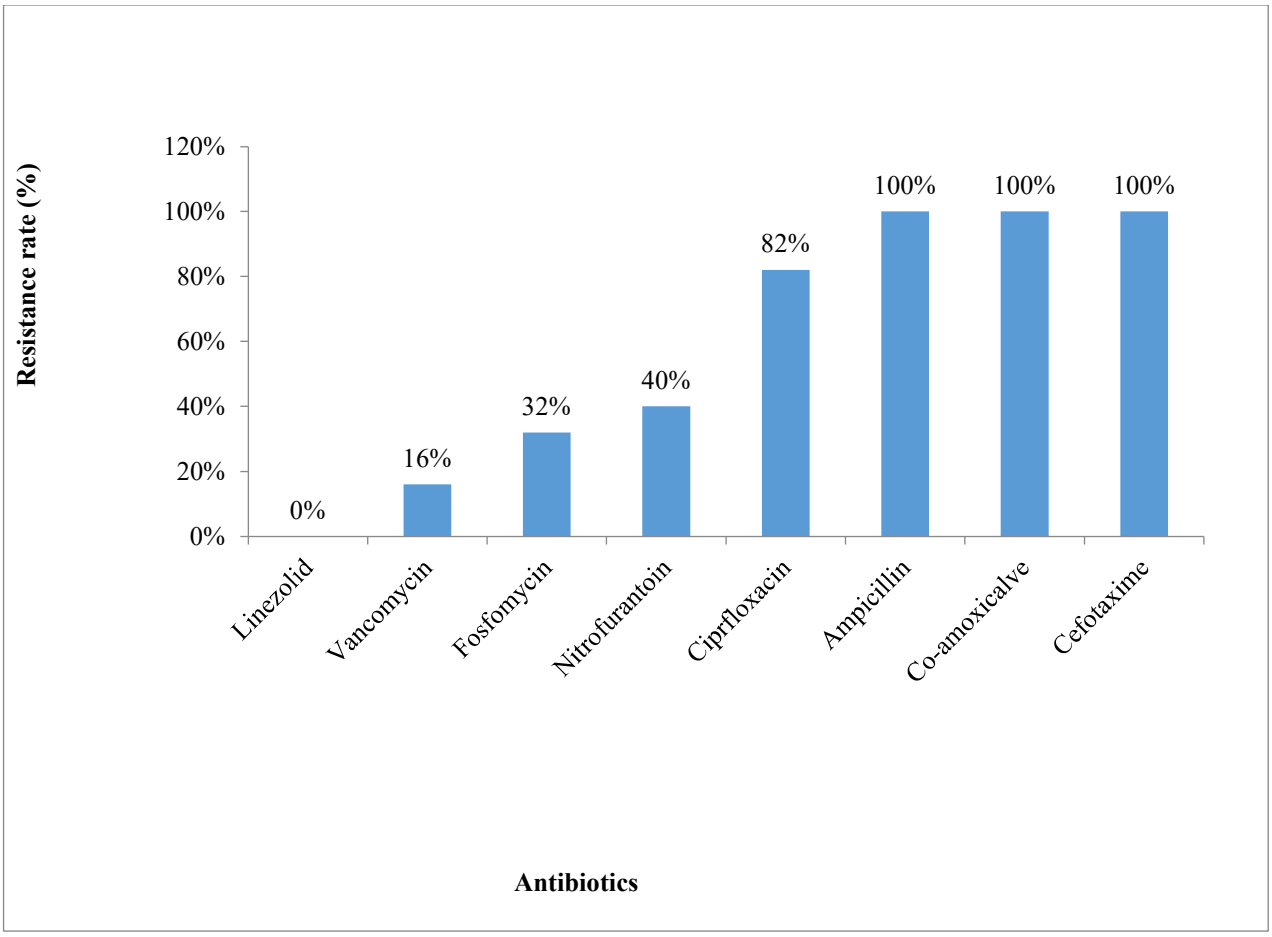


**Fig. 5**: Antimicrobial susceptibility profile of Enterococci

Another five-years study from Pakistan reported the top four GNR *E.coli, Klebsiella pneumoniae, P. aeruginosa* and *A. baumannii* (Rasool *et al*., 2019). Notably, during the course of this study however, the prevalence of *E. coli*, *Klebsiella spp.* And *P. aeruginosa* remained same the *M. morganii* has replaced the *A.baumannii* from forth most common GNR for UTIs. Here we report the emergence of *M. morganii* (9.32%) compared to *A. baumannii* (4.10%) as the fourth leading cause of UTIs which is noteworthy and requires more clinical vigilance. We also propose that this negligent rare opportunistic pathogen is ringing bells and fighting for recognition and should be considered as a next superbug for UTIs (Bandy, 2020). Recently UTIs due to *M. morganii* has been associated with immunosuppression and nephrotic syndrome comorbidity in children (Shi *et al*., 2022). Nearly half of Gram positive bacteria (46%) were identified as *Enterococci* in this study. *Enterococcus* species identification revealed *E. faecium* 74.89%, the most prevalent *Enterococci* followed by *E. faecalis* 18.61%, *E. gallinarum* 4.54% and *E. casseliflavus* 1.94%. Contrary to many investigations, *E, faecium* was the predominantly isolated *Enterococci* in our study (Akhter *et al*., 2014, Jahansepas *et al*., 2018). This might be explained in lieu of recent progress in *Enterococcal* genomic information that *E. faecium* isolates harbor a broader spectrum of virulence determinants compared to *E. faecalis* isolates (Aarestrup *et al*., 2000) and *E. faecium* is significantly more resistant organism than *E. faecalis* (Akhter *et al*., 2014).

AST revealed 16.39% *Enterococcus* isolates were VRE and predominant number of VRE were isolated from admitted patients. The pooled prevalence of VRE in Asia has been estimated 8.10% (Shrestha *et al*., 2021). A systematic review of past decade from Pakistan reported the vancomycin resistance 10.5% (Bilal *et al*., 2021). According to this study vancomycin resistance rate has increased from 8.10 to 16.39% which highlights the injudicious local prescriptions and calls for potential changes to curb the spread of resistance. Recently a cross-sectional study from Pakistan reported the resistance rate against ciprofloxacin (71.4%), nitrofurantoin (24.7%), fosfomycin (44.6%), ampicillin (44.8%), co-amoxiclav (45.6%) and linezolid (1.1%). In contrast we estimated very high resistance rate against ciprofloxacin 82%, nitrofurantoin 40.39%, fosfomycin (32%), ampicillin and co-amoxiclav (each 100%) and low resistance rate against fosfomycin 32.45% and linezolid (0%) (Idrees *et al*., 2022). Our results are similar to another comprehensive study from Pakistan which report resistance rate against

ciprofloxacin (85%), nitrofurantoin (54.5%), fosfomycin (21.5%), ampicillin (44%) and linezolid (0%) (Bilal *et al*., 2021). In this study, none of the *E. gallinarum* or *E. casseliflavus* were resistant to vancomycin and all of the VRE were identified as *E. faecium* or *E. faecalis*. Phenotypic classification revealed all of the vancomycin-resistant *E. faecium* isolates were resistant to teicoplanin indicating the presence of *vanA* gene alone or both *vanA* gene and *vanB* gene while 20% (06/30) *E. faecalis* isolates were only resistant to vancomycin and susceptible to teicoplanin indicating the presence of only *vanB* gene.

## CONCLUSION

UTIs remain the frequent clinical diagnosis in Pakistan. In this study, the prevalence of UTIs was 22% to which reproductive-age women and elders affected commonly. Predominant Gram negative urinary pathogens were *E. coli*, *Klebsiella spp.*, *P. aeruginosa* and *M. morganii* while *Enterococci* were the leading Gram positive pathogen. *E. faecium* were the most prevalent *Enterococci* followed by *E. faecalis* and motile *Enterococci.* VRE have spread around the globe and vancomycin resistance rate has increased by two-fold in Pakistan. All *E. faecium* exhibited VanA phenotype while 20% *E. faecalis* revealed VanB phenotype. We recommend focusing on (VanRS system) for a potential target of novel therapeutics to encounter the unexpected rapid spread of VRE.

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***Authors' contributions***
RMAK: Study conception and design, data acquisition and analysis, interpretation, critical revision, drafting, final approval.
AN: Data analysis, data acquisition, drafting, critical revision, interpretation, final approval.
MI: Data analysis, Critical revision, interpretation, drafting, final approval
QA: Data analysis, interpretation, drafting, final approval
SSH: Data acquisition, Data analysis, interpretation, critical revision, final approval
SJ: Data analysis, critical revision, drafting, interpretation, final approval
RM: Data acquisition, data analysis, interpretation, final approval.

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***Data availability statement***
We have provided all data in the form of references and figures and further will be provided on request.

***Ethical approval***
Ethical approval was obtained from the Ethical Review Committee (ERC) of the Sindh Institute of Urology and Transplantation (approval No. SIUT-ERC-2024/A-477).

***Conflict of interest***
The authors declared no conflict of interest

## REFERENCES

Aarestrup FM, Agerso Y, Gerner–Smidt P, Madsen M and Jensen LB (2000). Comparison of antimicrobial resistance phenotypes and resistance genes in *Enterococcus faecalis* and *Enterococcus faecium* from humans in the community, broilers and pigs in Denmark. *Diagn. Microbiol. Infect. Dis.,* **37**: 127-137.

Akhter J, Ahmed S and Anwar S (2014). Antimicrobial susceptibility patterns of Enterococcus species isolated from urinary tract infections. *BJMM.,* **8**: 16-20.

Bandy A (2020). Ringing bells: Morganella morganii fights for recognition. *Public Health,* **182**: 45-50.

Bano K, Khan J, Begum R, Munir S, Akbar N, Ansari JA and Anees M (2012). Patterns of antibiotic sensitivity of bacterial pathogens among urinary tract infections (UTI) patients in a Pakistani population. *Afr J Microbiol Res.,* **6**: 414-420.

Bilal H, Khan MN, Rehman T, Hameed MF and Yang X (2021). Antibiotic resistance in Pakistan: A systematic review of past decade. *BMC infectious diseases,* **21**: 244.

Biswas R, Rabbani R, Ahmed HS, Sarker MAS, Zafrin N and Rahman MM (2014). Antibiotic sensitivity pattern of urinary tract infection at a tertiary care hospital. *Bangladesh Crit Care J.,* **2**: 21-24.

Cheng B, Zaman M and Cox W (2022). Correlation of pyuria and bacteriuria in acute care. *AJM.,* **135**: e353-e358.

Facklam R and Collins M (1989). Identification of Enterococcus species isolated from human infections by a conventional test scheme. *J Clin Microbiol.,* **27**: 731-734.

Gaur P, Hada V, Rath RS, Mohanty A, Singh P and Rukadikar A (2023). Interpretation of antimicrobial susceptibility testing using European Committee on Antimicrobial Susceptibility Testing (EUCAST) and Clinical and Laboratory Standards Institute (CLSI) breakpoints: Analysis of agreement. *Cureus,* **15**(3): e36977.

Hussain N, Mahmud M, Anwar M and Wasim A (2020). Antimicrobial Susceptibility Pattern of Urine Culture Isolates in a Tertiary Care Hospital of Karachi, Pakistan. *J Health Med Sci.,* **3**(3): 393-400.

Idrees MM, Rasool MF, Imran I, Khalid A, Saeed A, Ahmad T and Alqahtani F (2022). A cross-sectional study to evaluate antimicrobial susceptibility of uropathogens from South Punjab, Pakistan. *Infect. Drug Resist.*, 1845-1855.

Jahansepas A, Aghazadeh M, Rezaee MA, Hasani A, Sharifi Y, Aghazadeh T and Mardaneh J (2018). Occurrence of *Enterococcus faecalis* and *Enterococcus faecium* in various clinical infections: Detection of their

drug resistance and virulence determinants. *Microbial Drug Resistance,* **24**: 76-82.

Khan E, Sarwari A, Hasan R, Ghori S, Babar I, O'brien F and Grubb W (2002). Emergence of vancomycin-resistant *Enterococcus faecium* at a tertiary care hospital in Karachi, Pakistan. *J. Hosp. Infect.,* **52**: 292-296.

Khan RMA and Pirzada ZA (2015). Emerging *Enterococcus gallinarum* infections and its antibiotic resistance in Karachi, Pakistan. *WJPS*, pp.658-662.

Khandelwal N, Panwala T and Patel JS (2020). Prevalence of enterococcus species and its vancomycin resistance pattern in a tertiary care hospital, Surat, Gujarat, India: A growing threat. *Blood,* **19**: 13.

Kwon YE, Oh DJ, Kim MJ and Choi HM (2020). Prevalence and clinical characteristics of asymptomatic pyuria in chronic kidney disease. *Ann Lab Med.,* **40**: 238-244.

Nadeem S, Badawy M, Oke OK, Filkins LM, Park JY and Hennes HM (2021). Pyuria and urine concentration for identifying urinary tract infection in young children. *Pediatrics,* **147**: e2020014068.

Najar M, Saldanha C and Banday K (2009). Approach to urinary tract infections. *Indian J. Nephrol.,* **19**: 129-139.

Rasool MS, Siddiqui F, Ajaz M and Rasool SA (2019). Prevalence and antibiotic resistance profiles of Gram negative bacilli associated with urinary tract infections (UTIs) in Karachi, Pakistan. *Pak J Pharma Sci.,* **32**(6): 2617-2623.

Raza T, Ullah SR, Mehmood K and Andleeb S (2018). Vancomycin resistant enterococci: A brief review. *J. Pak. Med. Assoc.,* **68**: 768-772.

Schmiemann G, Hoffmann F, Hamprecht A and Jobski K (2022). Patterns and trends of antibacterial treatment in patients with urinary tract infections, 2015-2019: An analysis of health insurance data. *BMC primary care,* **23**: 204.

Selim S (2022). Mechanisms of gram-positive vancomycin resistance. *Biomedical reports,* **16**: 7.

Sherman JM (1937). The streptococci. *Bacteriolo. Rev.,* **1**: 3-97.

Shi H, Chen X, Yao Y and Xu J (2022). Morganella morganii: An unusual analysis of 11 cases of pediatric urinary tract infections. *J Clin Lab Anal.,* **36**: e24399.

Shrestha S, Kharel S, Homagain S, Aryal R and Mishra SK (2021). Prevalence of vancomycin-resistant enterococci in Asia—A systematic review and meta-analysis. *J Clin Pharm Ther.,* **46**: 1226-1237.

Silva A, Costa E, Freitas A and Almeida A (2022). Revisiting the frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections. *Antibiotics,* **11**: 768.

Stogios PJ and Savchenko A (2020). Molecular mechanisms of vancomycin resistance. *Protein Science,* **29**: 654-669.

Tang SS, Apisarnthanarak A and Hsu LY (2014). Mechanisms of β-lactam antimicrobial resistance and epidemiology of major community-and healthcare-associated multidrug-resistant bacteria. *Adv. Drug Deliv. Rev.,* **78**: 3-13.

Ullah O, Khattak M, Hasan F, Raja N, Hussain S, Akhtar N and Shah AA (2015). Vancomycin resistant enterococcal infections in tertiary care hospitals of Islamabad and Rawalpindi, Pakistan. *Pak J Zool.,* **47**: 1503-1510.

Vasudevan R (2014). Urinary tract infection: An overview of the infection and the associated risk factors. *J Microbiol Exp,* **1**: 00008.

Wada Y, Irekeola AA, Ear ENS, Yusof W, Lih Huey L, Ladan Muhammad S, Harun A, Yean CY and Zaidah AR (2021). Prevalence of vancomycin-resistant Enterococcus (VRE) in companion animals: The first meta-analysis and systematic review. *Antibiotics,* **10**: 138.