Isolated Gram positive bacteria from patients infected with pyelonephritis chronic and acute in Al-Najaf Governorate, Iraq

Dhafer Rahman Abed Al-janabi[1] Email[1]: dhafer.rahmaan@iunajaf.edu.iq
Ahmed Abduljabbar Jaloob Aljanaby[2] Email[2]: ahmedjaloob@googlemail.com

[1]The Islamic University of Najaf, College of Medical Technology, Department of Renal Dialysis Technology, Iraq
[2] Department of Biology, Faculty of Science, University of Kufa, Iraq

Abstract:

Background: Pyelonephritis is one of the most common kidney diseases, and has serious complications. The purpose of this study was to investigate the presence of multidrug-resistant Gram-positive bacteria in patients with acute and chronic Pyelonephritis, as well as to test the antibiotic for the purpose of preventing Gram-positive bacteria infections.

Methods We isolated and detected bacteria from the urine of 348 patients with nephritis in our hospital from January 2023 to April 2024. All isolated bacterial strains were identified and tested by conventional culture methods, after which only positive bacteria were studied.

Results: We collected 348 samples from patients for pylonephritis , including 106 patients with Gram-positive bacteria of different sexes and ages, distributed as 60 acute and 46 chronic. The number of bacterial isolates was 110, belonging to the species *Staphylococcus aureus 28 (25.45%), Staphylococcus saprophyticus 31 (28.18%), Staphylococcus epidermidis11 (10%), Streptococcus agalactiae 17 (15.45%), Enterococcus faecalis 16 (14.55%), Corynebacterium urealyticum7 (6.36%),*.Ten types of antibiotics were tested, namely Augmentin,Amikacin, Trimethoprim, Imipenem, LevofloxacinPenicillin, Vancomycin, Ceftriaxone, Clarithromycin, Rifampicin.

Conclusions: *S. saprophyticus* and *S. aureus* were the major pathogens causing pyelonephritis in patients with Gram-positive bacterial infections and most of the isolates were sensitive to Imipenem and Vancomycin. Males were more susceptible than females and the age groups (30-49) and (50-69) years were more the most affected.

Keywords: Gram positive bacteria, Antibiotic and pyelonephritis

Abbreviations: urinary tract infection (UTI), acute pyelonephritis (APN), Chronic pyelonephritis (CPN), AMC= Augmentin, AK= Amikacin, TM= Trimethoprim, IMP= Imipenem, LEV= Levofloxacin, P= Penicillin, VA= Vancomycin, CRO= Ceftriaxone, CLM= Clarithromycin, RA= Rifampicin.

1 Introduction:

Pyelonephritis is an inflammation caused by bacteria that primarily effects the interstitial area and the renal pelvis or, less often, the renal tubules [1], [2]. It is one of the most common renal diseases, pyelonephritis cases are classified to acute and chronic [3]. To diagnose pyelonephritis, physicians must rely on evidence of urinary tract infection (UTI) from urinalysis and culture, along with signs and symptoms suggesting upper urinary tract infection (fever, chills, flank pain, nausea, vomiting, and costovertebral angle tenderness) Classification

of pyelonephritis acute and chornic Pyelonephritis. [4]. *Staphylococcus aureus* has been recognized as an important human pathogen and is the major cause of nosocomial infections, skin diseases, fatal pneumonia and osteomyelitis [5].The virulence of these bacteria occurred by secretion of toxins and enzymes which act on host cell membrane and mediated the cell destruction.[6] **.***Staphylococcus epidermidis* is the leading cause of hospital-acquired bloodstream, pyelonephritis, eye, ear, nose, wound and throat infections, Polysaccharide capsule allows them to adhesion to the surface and to form biofilm which decreases the metabolic activity of bacteria within them, *S. epidermidis* strains are often resistant to some antibiotics, such as penicillin, amoxicillin and methicillin (Visciano *et al.*, 2014; Alonso *et al.*, 2017). *Staphylococcus saprophyticus is part of the normal human flora that colonizes the perineum, rectum, urethra, cervix, and gastrointestinal tract*[8]. *The virulence factors of S. saprophyticus include adherence to urothelial cells by means of a surface-associated protein, lipoteichoic acid; a hemagglutinin that binds to fibronectin, a hemolysin; and production of extracellular slime* [9]. Strains belonging to *S. agalactiae* are described as (α), (β) or non-haemolytic (γ) when cultured on blood agar. It is part of the normal bacterial flora colonizing the gastrointestinal (GI) tract and genitourinary tract of a significant proportion of the human population. However, it occasionally becomes an infectious pathogen colonizing the uterus, blood, brain, and meninges [10].*Enterococcus faecalis* normally a gut commensal, is afrequent cause of many serious human infections, including .urinary tract infections are the most common, responsible for approximately 110,000 cases yearly, many of which are nosocomial (Kline and Lewis, 2017). possesses certain virulence factors including lytic enzymes, aggregation substance, pheromones and lipoteichoic acid (Lebreton, Willems and Gilmore, 2014).[11]. possesses certain virulence factors including lytic enzymes, aggregation substance, pheromones and lipoteichoic acid [12]. *Corynebacterium spp* is non-spore forming, gram positive bacilli, urease positive .It has been associated with acute or chronic encrusted UTI manifested by alkaline urine PH and crystal formation (Peiffer *et al.*, 2021; Salimiyan *et al.*, 2021). Isolation of this organism was rarely observed in a population of hospitalized patients [15].

2 Materials and Methods:

2-1 Study subjects

The current study in the advanced Microbiology Laboratory in the Department of biology/College of Science, University of Kufa was conducted by taking clinical samples urine from 348 patients with acute and chronic pyelonephritis, including females and males, aged between 10-89 years, who attended Hospital Al-Sadr Teaching Urology Department in Najaf Governorate,Iraq from January 2023 to April 2024. All patients were diagnosed by specialist doctor's urologist of unit depending on history and clinical examinations and ultrasound.

All urine samples were collected and dignosis according [16] [17]were confirmed by Vitek system (BioMerieux, Lyon, France). Antimicrobial susceptibility profile was determined by the interpretation of the breakpoints recommended by the Clinical and Laboratory Standards Institute (CLSI) . company of antibiotic discs(Bioanalysis Company / Turkia) . The study was approved by the of Kufa and the Scientific Committee for Research in the Health Department of Najaf (N.34469-2023)

2-2 Statistical analysis: SPSS statistical package version 26 Statistical significance was accepted at P-Value <0.05. [18] .

3-Results:

The results showed that positive bacteria causing pyelonephritis were present in 106/348 (30%45) and negative bacteria were 242 (69.54%) as shown in Figure (1). According to Figures (2 and 3) which show the number of cases, acute pyelonephritis was 60/106 (56.6%) and chronic pyelonephritis was 46/106 (43.4%), the number of males was 56/106 (52.83%) and the number of females was 50/106 (47.17%). As for ages, they were divided into four categories as shown in Table (1): age group (10-29 years) 11 (10.37%), age group (20-49 years) 40 (37.73%), age group (50-69 years) 39 (36.79%) and age group (70-89 years) 16 (15.09%). There were 4/106 (3.77%) samples of patients with pyelonephritis who had a common bacterial growth and 102/106 (96.23%) had a single growth figure (4) and the common isolates were as shown in Table (2). (*S.saprophyticus* + *S.aureus*), 2 samples (40%) ,and only one isolate (20%) for(*E. . faecalis* + *S. epidermidis*),(*S.saprophticus* + *St.agalactiae*),(*S.aureus* + *St. agalactiae*).Thus, the number of positive bacterial isolates was 110 isolates for the number of patients 106 patients and they belonged to six bacterial species which are *Staphylococcus aureus*28 (25.45%)., *Staphylococcus saprophyticus*31 (28.18%)., *Staphylococcus epidermidis*11 (10%)., *Streptococcus agalactiae* 17 (15.45%)., *Enterococcus faecalis*16 (14.55%)., *Corynebacterium urealyticum*7 (6.36%). distributed depending on the type of disease, gender and age according to Tables (3, 4 and 5 respectively). Table (6) shows the sensitivity test of antibiotics for positive bacteria isolated from pyelonephritis.

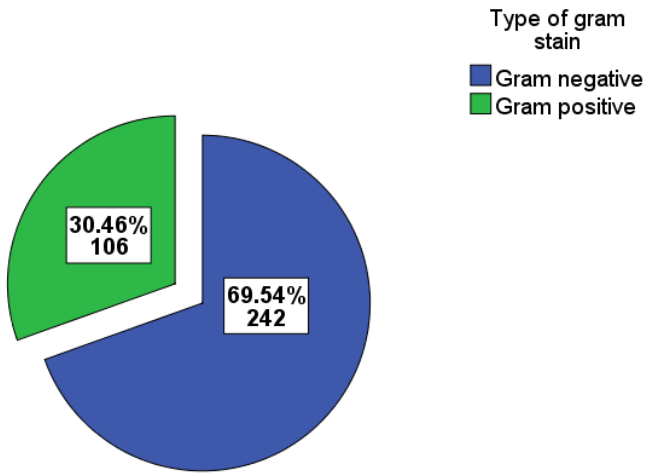

Figure (1): Numbers and percentages of positive bacteria compared to negative bacteria for pyelonephritis patients (total sample =348)

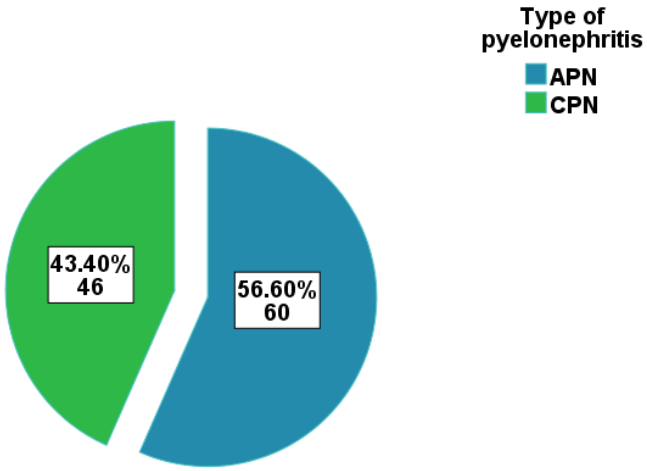

Figure (2): Numbers and percentages of Acute pyelonephritis (APN) and Chronic pyelonephritis (CPN) (P-Value =0.096)

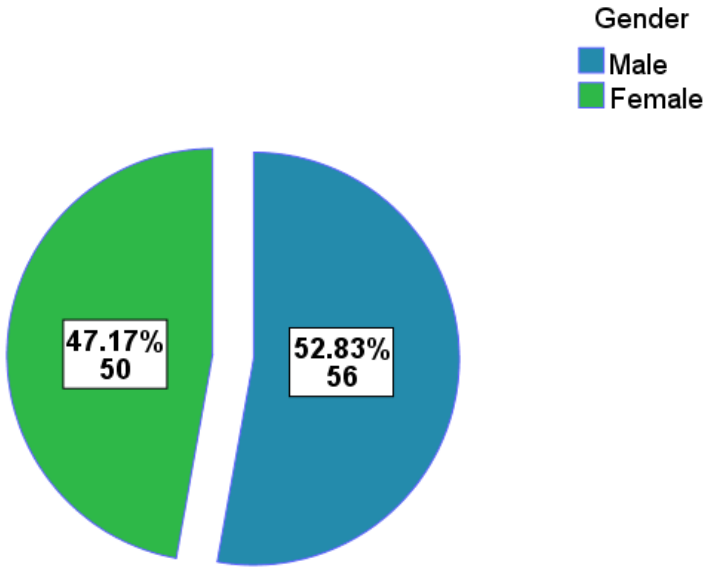

Figure (3): Numbers and percentages patients infected with pyelonephritis according to sex. (P-Value =0.764)

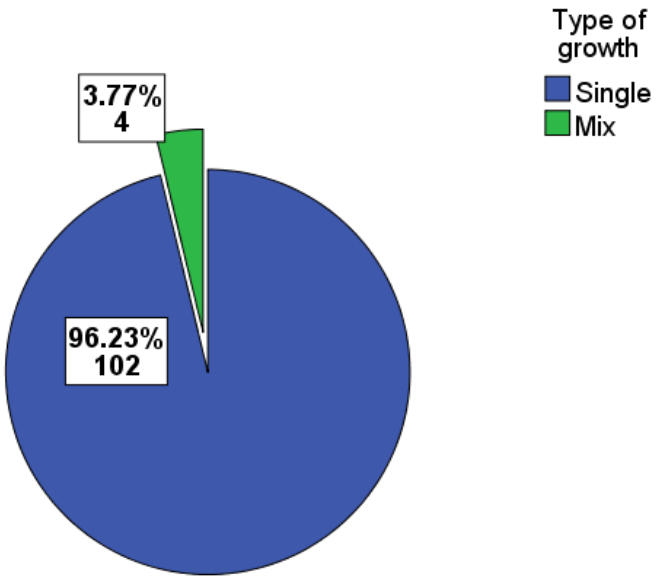

Figure (4): Numbers and percentages patients infected with pyelonephritis according to growth. (P-Value =<0.001*)

Table:1 Numbers and percentages of types of pyelonephritis patients according to sex and age(N=106).

Age / Years	Acute pyelonephritis				Chronic pyelonephritis				Total	
	Female		Male		Female		Male			
	Count	%	Count	%	Count	%	Count	%	Count	%
(10-29)	4	3.8%	2	1.9%	2	1.9%	3	2.8%	11	10.37
(30-49)	11	10.4%	15	14.2%	8	7.5%	6	5.7%	40	37.73
(50-69)	12	11.3%	12	11.3%	7	6.6%	8	7.5%	39	36.79
(70-89)	3	2.8%	1	0.9%	3	2.8%	9	8.5%	16	15.09
Total	30	28.30%	30	28.30%	20	18.87%	26	24.53%	106	100%

Table: 2 Mixed bacterial species for patients pyelonephritis

Type of bacteria	Acute				Chronic				Total	
	Female		Male		Female		Male			
	Count	%	Count	%	Count	%	Count	%	Count	%
E. faecalis + S.epidermidis	0	0.0%	0	0.0%	0	0.0%	1	20.0%	1	20%
S. aureus + S.saprophyticus	0	0.0%	0	0.0%	1	20.0%	1	20.0%	2	40%
S. aureus + St.agalactiae	1	20.0%	0	0.0%	0	0.0%	0	0.0%	1	20%
S.saprophyticus + St. agalactiae	0	0.0%	1	20.0%	0	0.0%	0	0.0%	1	20%
Total	1	20%	1	20%	1	20%	2	40%	5	100%

Table: 3 Total of bacterial according to type of pyelonephritis

Type of bacteria	Acute		Chronic		Total	
	Count	%	Count	%	Count	%
E. faecalis	12	10.91	4	3.64	16	14.55
S. aureus	10	9.09	18	16.36	28	25.45
S.saprophyticus	24	21.82	6	5.45	30	27.27
S. epidermidis	0	0.00	12	10.91	12	10.91
C. urealyticum	0	0.00	7	6.36	7	6.36
St. Agalactiae	16	14.55	1	0.91	17	15.45
Total	62	56	48	44	110	100

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Table: 4 Distribution of bacterial isolated from patients with pyelonephritis according to sex groups

Type of bacteria	Sex					
	Female		Male		Total	
	Count	%	Count	%	Count	%
E. faecalis	8	7.27	8	7.27	16	14.55
S. aureus	12	10.91	16	14.55	28	25.45
S.saprophyticus	15	13.64	16	14.55	31	28.18
S. epidermidis	6	5.45	5	4.55	11	10.00
C. urealyticum	4	3.64	3	2.73	7	6.36
St. Agalactiae	7	6.36	10	9.09	17	15.45
Total	52	47.27	58	52.73	110	100

Table: 5 Distribution of bacterial isolated from patients with pyelonephritis according to age groups

Type of bacteria	Age / Years (10-29)		(30-49)		(50-69)		(70-89)		Total	
	Count	%	Count	%	Count	%	Count	%	Count	%
E. faecalis	1	0.91	7	6.36	5	4.55	3	2.73	16	14.55
S. aureus	3	2.73	12	10.91	10	9.09	3	2.73	28	25.45
S.saprophyticus	3	2.73	12	10.91	15	13.64	1	0.91	31	28.18
S. epidermidis	2	1.82	1	0.91	3	2.73	5	4.55	11	10.00
C. urealyticum	1	0.91	3	2.73	1	0.91	2	1.82	7	6.36
St. agalactiae	1	0.91	7	6.36	6	5.45	3	2.73	17	15.45
Total	11	10	42	38	40	36	17	15	110	100

Table: 6 Total gram positive bacteria isolated from pyelonephritis were resistant to antibiotics.N=106

Antibiotic	*E. faecalis 16 (100%)*	*S. aureus 28 (100%)*	*S. saprophyticus 31 (100%)*	*S. epidermis 11 (100%)*	*St. agalactiae 17 (100%)*	*C. urealyticum 7 (100%)*
AMC	16 (100)	26 (92.85)	31 (100)	3 (27.2)	16 (94.11)	5 (71.43)
AK	4 (25)	7 (25)	5 (16.12)	2 (18.18)	3 (17.64)	0 (00)
TM	11 (68.75)	20 (74.42)	27 (87.09)	5 (45.44)	4 (23.52)	4 (57.14)
IMP	4 (25)	15 (53.57)	3 (9.6)	2 (18.18)	1 (5.88)	0 (00)
LEV	9 (56.25)	15 (53.57)	9 (29.03)	4 (36.36)	3 (17.64)	2 (28.57)
P	16 (100)	28 (100)	28 (90.3)	11 (100)	17 (100)	5 (71.43)
VA	3 (18.75)	6 (21.42)	8 (25.8)	1 (9.09)	2 (11.76)	1 (14.29)
CRO	16 (100)	12 (42.85)	23 (74.19)	3 (27.2)	5 (29.41)	4 (57.14)
CLM	3 (18.75)	26 (92.85)	31 (100)	11 (100)	13 (76.47)	3 (42.86)
RA	10 (62.5)	17 (60.71)	22 (70.95)	10 (90.9)	8 (47.05)	2 (28.57)

Data presented as numbers and percentage of pathogenic bacterial isolates that were resistant to antimicrobials: AMC= Augmentin, AK= Amikacin, TM= Trimethoprim, IMP= Imipenem, LEV= Levofloxacin, P= Penicillin, VA= Vancomycin, CRO= Ceftriaxone, CLM= Clarithromycin, RA= Rifampicin.

4 Discussion:.

Demographic characteristics of study groups

Pyelonephritis, one of the most prevalent kidney diseases in developing countries, is recognized as an important public health concern for healthcare systems worldwide [19]. The rate of chronic kidney infection was higher than acute kidney infection. In Iraq, there are not many studies to compare them or study them together, especially in Najaf Governorate, so this study is the first according to what I have seen. The reason may be due to patients not visiting the hospital or specialist doctor except in very dangerous and difficult cases, and thus infection is possible. The disease may change from acute to chronic [20]. In addition to chronic disease, it is more common in people due to weak immunity or the accumulation of other diseases [21].The results of this study were consistent with the results of a study Umesha *et al,* conducted in Indian (2018), where it was found that the infection rate in males was 65.88 % while in females it is 34.12% .Acute pyelonephritis in males is more prevalent in older ages than at other ages, and this may be due to some factors such as prostate enlargement (causing urethral obstruction with incomplete emptying) [22], Activity in prostatic secretions may lead to urinary tract infection in aging males [23]. While the age most commonly affected in females is parenthood, it may be because multiple factors such as pregnancy, sexual activity, and urogenital changes in adulthood may increase susceptibility to uppre or lower urinary tract in females [24] . pyelonephritis have been described as an important infectious pathology in patients of in all age groups infants, children, adults and the elderly , and both sexes [25]. Nevertheless,pyelonephritis is most common between males although with around two-thirds of women in experiencing a UTI at least once during their lifetime [26].

Gram positive bacteria

Staphylococcus saprohytica is considered the most common Gram-positive bacteria in the urine of patients with pyelonephritis. were isolated from acute infections and chronic infections. These results are consistent with [27]. Coagulase-negative staphylococci (CoNS), as part of the skin and mucous membrane microbiota, are often considered simple commensal bacteria and are frequently viewed as contaminants when identified in cultures [28]. A Japanese multicenter prospective study found that CoNS (3.8%) were isolated in patients with obstructive pyelonephritis due to urolithiasis (Hayano *et al.*, 2024). *Staphylococcus saprophyticus* has been identified as a common microorganism in uncomplicated lower urinary tract infections in young, sexually active women [30], and has many different virulence factors such as Aas adhesin, Ssp adhesin, SdrI adhesin, and Uaf adhesin) as adherence factor, although it contains Aas toxin and urease enzyme [31]. Lower urinary tract infections caused by S.saprophyticus are more likely to occur in sexually active men and women [32]. In general, when *S.saprophyticus* contaminates the vaginal area, it ascends through the urinary tract to the upper part [33]. In the process of ascension, *S.saprophyticus* uses citrate in urine to synthesize carboxylate siderophores and obtain iron ions in urine to provide it with nutrition and growth (Souza *et al.*, 2019). This study revealed that was ***Staphylococcus aureus*** isolates from urine infected with pyelonephritis.These results in agreement with [35]. *Staphylococcus aureus* is a significant human pathogen responsible for most cases of nosocomial and hospital acquired infections. It is responsible for the occurrence of several diseases (Rasheed and Hussein, 2021; Altaher, Shahlol and Ahmed, 2023), and is a relatively causative agent of urinary tract infection (UTI) [38] . However, the clinical features of *S. aureus*-related UTI are unclear [39]. Paying attention to risk factors, specifically indwelling catheterization, renal stones, and hydronephrosis, will be an effective strategy for prevention of UTI [40]. *Staphylococcus aureus* is one of the most prevalen in the hospital environment, its high resistance against hard conditions and occurrence of high antibiotic resistance in some of its strains (Kholaseh, Derakhshan and Abedini, 2023), and have the capacity to adhere to several different surfaces including abiotic (polyethylene, stain steel, rubber, and glass) or biotic surfaces (living tissue or abiotic surfaces covered with proteins) [9], also bacterial adhesion is facilitated

by a different set of interactions, mostly by ligand–receptor specific interactions between host cells or extracellular matrix proteins and bacterial surface-associated adhesins [42]. I believe that for the reasons mentioned above, it is one of the bacterial types that cause pyelonephritis. ***Staphylococcus epidermidis*** was present in chronic pyelonephritis only usually considered to be a contaminant in urine cultures . Therefore, *S. epidermidis* should not be ignored in any study and considered as a contaminant, especially in the case of a patient who suffers from symptoms with repeated positive urine cultures as our results showed, all of them were in chronic cases, the possibility of a urinary tract infection must also be taken into account. ***Enterocous faecalis*** is one of the most resistant gram-positive bacteria in pyelonephritis, which has caused great trouble for clinical treatment [43]. *Enterococcus faecalis* have many virulence factors for example (Ebp pili: endocarditis- and biofilm-associated, Ace adhesin, Esp adhesin: enterococcal surface protein) as adherence factors, Epa: enterococcal polysaccharide antigen as immune evasion, also it has Sortase A, SigV, MsrA: methionine sulfoxide reductase A and MsrB: methionine sulfoxide reductase B [44], [45]. Invasive disease due to group B *Streptococcus* (GBS) infection (***Streptococcus agalactiae)*** has become cause of bacterial infections in the bacteraemia, amnionitis, endometritis, and urinary tract infection in pregnant women as well as focal and systemic infections in newborns [46] it is a relatively rare cause of infection in older children and non-pregnant adults [47]. Furthermore, *S. agalactiae* strains can grow in human urine, and this relates in part to malic acid metabolism [48]. GBS bacteriuria in women during pregnancy is a risk factor for late gestational maternal colonization with GBS and early-onset neonatal GBS infection. In men, GBS may be associated with prostatitis [49] . Showed that the presence of *S. agalactiae* in the urinary tract could predispose the host to other uropathogenic bacteria such as *E. coli* (Chan *et al*., 2019). In this study ***Corynebacterium urealyticum*** isolates of patients with the chronic pyelonephritis only and not faund in acute, *C. urealyticum* is an opportunistic nosocomial pathogen mainly causing acute cystitis, pyelonephritis, alkaline encrusted cystitis, and encrusted pyelitis and may also cause bacteremia in patients with chronic urological diseases [51] and causes UTIs including pyelonephritis and cystitis, encrusted pyelitis usually occurs, which can occur at any age [52]. Infection with C. urealyticum is uncommon in children but must be considered [53].

Antibiotic Sensitivity Test for Bacterial Isolates

Resistance to bacterial isolates in patients with pyelonephritis is considered one of the most important and greatest medical problems, [54],.The observed drug resistance of these bacteria is a potential indicator that the isolates were previously exposed to these antibiotics, which may have promoted the development of resistance and multidrug resistance [55], [56]. As for *S. aureus*, the cell wall is impermeable to drugs, β-lactamase activity, variable penicillin-binding proteins (PBPs) and modified genes found in some strains of *S. aureus* [57]. Penicillin and cephalosporin resistance of *S. aureus* isolates may arise as a result of changes in Components of the cell's outer membrane, such as proteins that form channels, and therefore do not allow the entry of antigens or other molecules [6], [58].The results showed that *S. saprophyticus* had resistance because strain-specific virulence strategies possessed the aggression, invasion and adherence factors necessary for pathogenicity and evaded host immune mechanisms. Once the periurethral area was contaminated with *S. saprophyticus* from the intestine, the microorganisms would colonize with the *staphylococci*. Urethra before movment to the bladder, to adhere to urothelial cells, *S. saprophyticus* expresses adhesins: extracellular slime and fibronectin-binding proteins [59], [60].*Staphylococci saprophyticus* strains can also produce urease that decomposes ammonia into ammonia and carbon dioxide, and ammonia will support bacterial survival as the pH increases [61]. Once the cells of the host immune system sense a bacterial infection, phagocytes, macrophages, and neutrophils are called upon to engulf the bacteria. The bacteria are then trapped

within the phagosome, which occurs when the phagosome fuses with a specialized vesicle containing lysis factors. However, *S. saprophyticus* can they eventually escape the digestion pocket and cover themselves with host proteins in order to mask themselves to prevent recognition by antibodies or blood proteins (Djawadi *et al.*, 2023).*Enterococcus faecalis* contains several virulence factors for example (Ebp pili: endocarditis and biofilm associated, Ace adhesin, Esp adhesin: enterococcal surface protein) as adherence factors, Epa: (enteropolysaccharide) antigen as immune evasion, they also contain Sortase A, SigV, MsrA: methionine sulfoxide reductase A and MsrB: methionine sulfoxide reductase B, and all of these virulence factors gave *E. faecalis* this resistance [62]. *Streptococcus agalactiae* may be able to produce a wide range of virulence factors, including toxins (beta-hemolysin/cytolysin and CAMP factor), and proteins that facilitate host cell adhesion, colonization, and invasion (fibrinogen-binding protein FbsA, αC protein, Rib protein, and HylB hyaluronidase) [63].

5 Conclusions

Pyelonephritis is a major public health problem worldwide in Najaf Governorate and affects all age groups and both sexes.There were more pyelonephritis in male than in female and the age group from 30 to 69 is most susceptible to the disease .The percentage of Gram- positive bacteria isolated from Pyelonephritis was less than that of Gram- negative bacteria. The common Gram-positive bacteria causes to urinary tract infection was S.*saprophyticus*. Gram- positive bacteria isolated from pyelonephritis has a great resistance to many commonly antibiotics and the highest rate of resistance the seen with Pencillin , whereas the low rate resistance was seen with Imipenem and Vancomycin.

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