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Assessment of Beta-lactamases and Integrons Genes among Bacteria Isolated From Bladder Cancer Patients with Urinary Tract Infections

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ABSTRACT

Background and Aim: One of the most dangerous side effects and the main factor in both morbidity and mortality in cancer patients are infections. Urinary tract infections (UTIs) are among the most prevalent infections in cancer patients. The Recent study aimed to isolation , identification of bacteria from bladder cancer patients with UTIs treated with BCG OR Mitomycin C (MMC) and characterized the presence of bla SHV , bla IMP by PCR in addition to detection the prevalence of Integron gene in the isolated bacterium .

Methods: Two hundred urine samples were taken from patients with bladder cancer one hundred from bladder cancer patients treated with BCG (Group-1) and one hundred treated with Mitomycin C (Group –II) between the dates of 1 April 2021 and 15 October 2021 while they were enrolled in third floor Ghazi Al- Hariri Hospital, Medical City, Baghdad Province, and private clinics in Nasiriyah Province. Forty urine samples were taken from patients with UTI without Bladder Ca (Control ,Group -III). Bacterial strains were identified using the Indole test ,Oxidase test , β-hemolytic activity, API20 E test and by 16sRNA .

Results: The most commonly pathogens were Escherichia coli , followed by Klebsiella pneumoniae , Pseudomonas aeruginosa and Staphyllococcus aureus and other genera of UTI bacterium. The total BlaSHV Producers in the current study from 38 isolates were 18 isolate(47.3%).The highest BlaSHV Producer in all Groups was E.coli followed by K.pneumoniae and P.aeruginosae . None of all tested isolates were positive to BlaIMP gene while the presence of Integron class 1 was detected in(34)89.4% of total isolates.

Keywords: *MBLs genes ,ESBLs genes , Integrons , Bladder Cancer ,UTI*

INTRODUCTION

The urinary bladder is a hollow, viscous, pyramid-shaped pelvic organ. The bladder's role is to store urine and aid in the evacuation of urine during micturition. It is located near other pelvic organs, such as the distal bowels (rectum) and organs from the male and female genital tracts (1). As the ninth most prevalent type of cancer overall, bladder cancer (Bca) is still the most common malignancy of the urinary system (2). With an anticipated 81,400 new cases and 4.5% of all new cancer cases in the US in 2020, it is the sixth most prevalent malignancy. One of the most dangerous side effects and the main factor in both morbidity and mortality in cancer patients are infections. Urinary tract infections (UTIs) are among the most prevalent infections in cancer patients (3). UTIs can range from asymptomatic bacteriuria to mild uncomplicated cystitis, potentially serious pyelonephritis, and even life-threatening sepsis. A number of microorganisms, primarily the Enterobacteriaceae, are responsible for UTIs (4). The most common bacterium is Escherichia coli, Other significant gram-negative bacterial species include Klebsiella and Proteus spp., Pseudomonas sp., and gram-positive strains like Enterococcus faecalis, as well as a few Staphyllococci species, such as Staphyllococcus epidermidis, Staphyllococcus aureus, and Staphyllococcus saprophyticus, the latter is restricted usually on female UTIs (5).The most common antibiotics that doctors recommend are beta lactams. A four-member, nitrogen-containing, β-lactam ring is the structural basis of beta-lactam antibiotics. The ring structure and connected chemical groups of the antibiotics vary. Penicillins, Cephalosporins, Carbapenems, and Monobactams are examples of β-lactam drug types. Even while urinary tract infections (UTIs) are treatable, antibiotic resistance among urinary tract bacteria has been on the rise, making it harder to keep under control. The synthesis of hydrolytic enzymes, known as "β-lactamases," is the most prevalent method of resistance among Enterobacteriaceae (6). The term "β-lactamases" refers to enzymes that break down the amide link in the β-lactam ring, inactivating the medicine and ending the treatment. Based on genetics, biochemical characteristics, and substrate affinity for a β-lactamase inhibitor, β-lactamases are classified in a complicated way. (7). According to their molecular makeup, β-lactamases can be divided into four different groups called classes A through D. Because Classes A, C, and D have a serine residue at the active site that causes bond hydrolysis, they are also known as serine β-lactamases (SBLs). Class A enzymes include the following: (1) TEM, which is the first plasmid-encoded β-lactamase identified in Gram-negative bacteria and is named for a patient by the name of Temoniera; (2) Sulfhydryl variant (SHV), an enzyme with similar activity to TEM; (3) Cefotaximase (CTX-M); and (4) K. pneumoniae carbapenemase (KPC), which is in charge of carbapenem (8). Class B β-lactamases, on the other hand, are known as metallo—β-lactamases (MBLs) because the hydrolytic action is boosted by one or two necessary zinc ions in the active sites (9). Class C comprises the AmpC β-lactamases, while classes A and D contain the classic and extended-spectrum β-lactamases (ESBLs) (ACBL) (10). MBLs are class B β-lactamases that can hydrolyze all β-lactam classes except monobactams (11). These enzymes are inhibited by metal chelators such as EDTA and thiolates. Verona integrin-encoded MBL (VIM), Imipenemase (IMP), and New Delhi MBL (NDM), among others, are the most widely used and clinically significant class B enzymes (12).

Horizontal gene transfer via mobile genetics components including plasmids, transposons, and integrons is the primary cause of the rise in antibiotic resistance (13). Open reading frames are incorporated into and transformed into functional genes by integrons, which are frequently used methods of gene capture and expression.

MATERIALS AND METHODS

Isolation and Detection of Gram Negative Bacteria

Two hundred urine samples were taken from patients with bladder cancer one hundred from bladder cancer patients treated with BCG (Group-1) and one hundred treated with Mitomycin C (Group –II) between the dates of 1 April 2021 and 15 October 2021 while they were enrolled in third floor Ghazi Al- Hariri Hospital,

Medical City, Baghdad Province, and private clinics in Nasiriyah Province. Forty urine samples were taken from patients with UTI without Bladder Ca (Control ,Group -III). Bacterial strains were identified using the Indole test ,Oxidase test , β-hemolytic activity, API20 E test and by 16sRNA .

Polymerase chain reaction (PCR)

Conventional PCR were used to amplify the target DNA using specific primer pairs for Molecular identification of E.coli ,K.pneumoniae and P.aeruginosae and BlaSHV,BlaIMP and Integron genes (Table 1)

Data Analysis

The Statistical Analysis System(14) program was used to detect the effect of difference factors in study parameters. Least significant difference – LSD test was used to significant compare between means. Chi-square ($\chi 2$) test was used to significant compare between percentage (0.05 and 0.01 probability) in this study.

TABLE 1: Primers used in identification of bacterial isolates and BlaSHV,BlaIMP and Integron genes.

Target Gene	Oligonucleotide Sequence (5'-3')	Amplicon Size (bp.)	Conditions	References
16sRNA E. coli	F: AGAGTTTGATCMTGGCTCAG R: CCGTCAATTCATTTGAGTTT	919 bp	Step 1: 94ºC, 30 sec.. Step 2: 94ºC, 15- 30 sec. Step 3: 57 ºC, 15- 60 sec. Step 4: 68ºC, 1 min/kb. Step 6: 68 ₒC, 5 min. Step 7: 4-10 ºC, forever	(15)
16sRNA K. pnuemuniae	F:GCAAGTCGAGCGGTAGCACAG R: CAGTGTGGCTGGTCATCCTCTC	216bp	Step 1: 94ºC, 30 sec.. Step 2: 94ºC, 15- 30 sec. Step 3: 55ºC, 15- 60 sec. Step 4: 68ºC, 1 min/kb. Step 6: 68 ₒC, 5 min. Step 7: 4-10 ºC, forever	(16)
16sRNA P.aeruginosa	F:TGCCTGGTAGTGGGGGATAA R:- GGATGCAGTTCCCAGGTTGA `	505 bp	Step 1: 94ºC, 30 sec.. Step 2: 94ºC, 15- 30 sec. Step 3: 57ºC, 15- 60 sec. Step 4: 68ºC, 1 min/kb. Step 6: 68 ₒC, 5 min. Step 7: 4-10 ºC, forever	(17)
Bla SHV	Bla SHV -F: GGA AAC GGA ACT GAA TGA GG Bla SHV -R: ATC CCG CAG ATA AAT CAC CA	301	Step 1: 94ºC, 30 sec.. Step 2: 94ºC, 15- 30 sec. Step 3: 55 ºC, 15- 60 sec. Step 4: 68ºC, 1 min/kb. Step 6: 68 ₒC, 5 min. Step 7: 4-10 ºC, forever	(18)
Bla IMP	F: GGAATAGAGTGGCTTAAYTCTC R: CCA AACYACTASGTTATCT	188	Step 1: 94ºC, 30 sec.. Step 2: 94ºC, 15- 30 sec. Step 3: 55 ºC, 15- 60 sec. Step 4: 68ºC, 1 min/kb. Step 6: 68 ₒC, 5 min. Step 7: 4-10 ºC, forever	(19)

Int 1	Int 1-F: 5′-GGTGTGGCGGGCTTCGTG-3′ Int 1-R: 5′-GCATCCTCGGTTTTCTGG-3′	480	Step 1: 94ºC, 30 sec.. Step 2: 94ºC, 15- 30 sec. Step 3: 53 ºC, 15- 60 sec. Step 4: 68ºC, 1 min/kb. Step 6: 68 ₀C, 5 min. Step 7: 4-10 ºC, forever	(20)

RESULTS

Bacterial isolation

The current study was conducted on 200 specimens from Bladder Carcinoma patients with Urinary Tract Infections and 40 specimens from non- bladder cancer Patients with UTIs .The results were distributed according to the patient's Bladder Ca. therapy . The incidence among patients treated with BCG was 33(33%) (Group-I) , while that for those treated with Mitomycin C(MMC.) Was 23 (23%)(Group-II).The incidence in Control samples (non-Bladder Ca. Patients but have UTIs.) was 17 (42.5 %) (Group-III) as observed in the (Table 2) (Figure 1). The most commonly pathogens were Escherichia coli , followed by Klebsiella pneumoniae , Pseudomonas aeruginosa and Staphyllococcus aureus and other genera of UTI bacterium from All three groups as represented in (Table 3) , the results showed significant differences ($p < 0.05$).

TABLE 2: Distribution of UTIs Patients according to the three groups

Patients with UTIs.	Isolates NO.	%
Group-I	33	33%
Group-II	23	23%
Group-II	17	42.5%

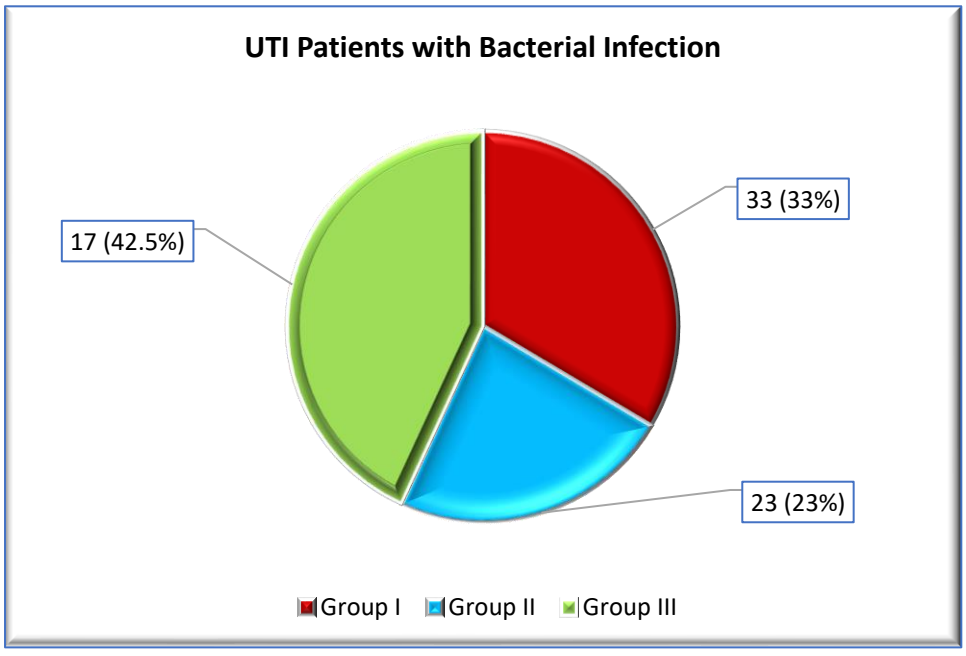

FIGURE 1: Percentage of bacterial isolation among the three groups

TABLE 3: Bacterial isolates from different three groups

Bacterial Species	Group-I		Group-II		Group-III		Total
	No.	%	No.	%	No.	%	No.
E. coli	13	13	9	9	4	10	26
K. pneumoniae	11	11	9	9	4	10	24
P. aeruginosa	5	5	3	3	2	5	10
S. aureus	4	4	2	2	1	2.5	7
Morganella. morgani	0	0	0	0	4	10	4
P. mirabilis	0	0	0	0	1	2.5	1
E. cloacae	0	0	0	0	1	2.5	1
Total	33	33	23	23	17	10	73
CalX2= 24.81	TabX2= 21.03			DF= 12		p. value 0.016*	

Bacterial Identification

The identification according to (21) On various media, including Blood agar, MacConkey agar, Eosin Methylene Blue (EMB), and Mannitol salt agar, the cultural traits of 73 isolates from All Groups were examined. Results showed that 26 isolates from all groups had E.coli growth. Twenty-four (24) isolates of K.pneumoniae from all groups .Ten (10) isolates of P. aeruginosa , seven (7) isolates of Staphylococcus aureus , four isolates of M. morganii, one strain of Proteus mirabilis and One isolate of Enterobacter cloacae . Biochemical tests were conducted on the predominant isolates in Groups I, II, and III, including E. coli, K. pneumoniae, and P. aeruginosa. Additional verification was performed using the API 20E system based on 20 biochemical assays related to the activities of E. coli ,K.pneumoniae and P.aeruginosae metabolism after 18 hours at 35°C .After that and by using a genomic DNA minikit, genomic and according to (22) ,DNA was isolated from 40 bacterial isolates, including E. coli (17), K. pneumonia (15), and P. aeruginosae (8) .Such results were also observed when the DNA samples analyzed by gel electrophoresis, in which DNA bands were detected indicating purified DNA samples as shown in (Figure 2 a& b).

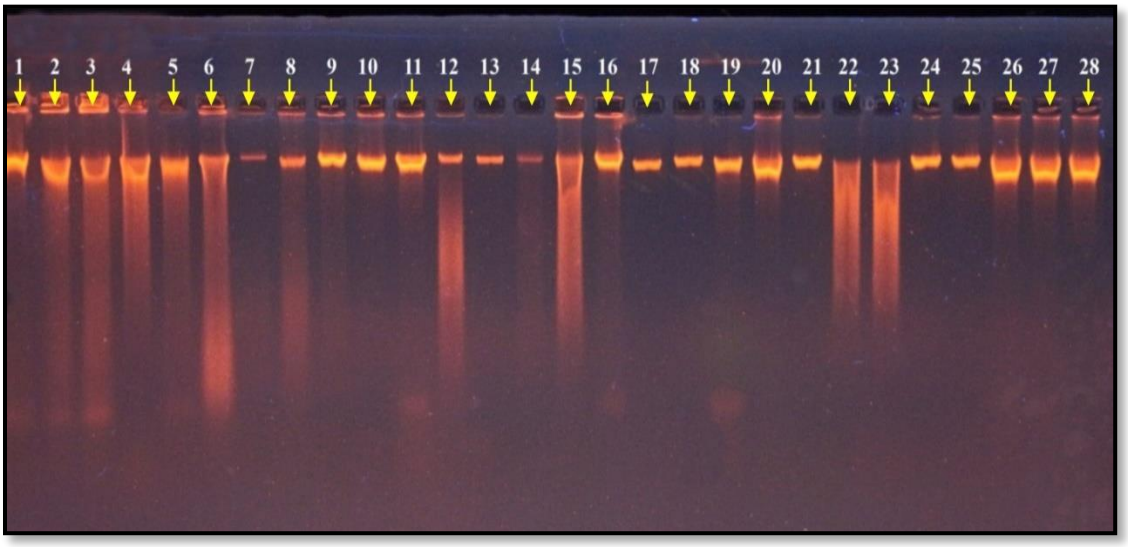

FIGURE 2 A: Ethidium Bromide stained agarose gel electrophoresis appearance that displays DNA from bacteria that was extracted.

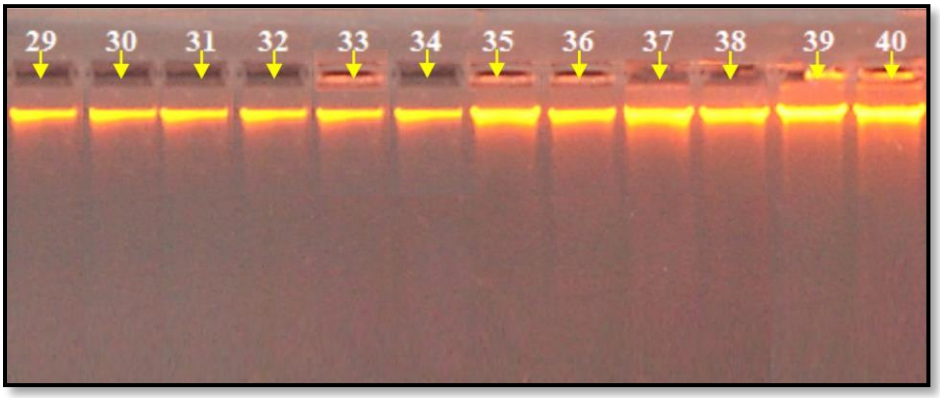

FIGURE 2 B: Ethidium Bromide stained agarose gel electrophoresis appearance that displays DNA from bacteria that was extracted.

Amplification of 16S rRNA gene

Using particular primers for the PCR amplification of E. coli, K. pneumonia, and P. aeruginosae 16S rRNA, 40 isolates were subjected to molecular identification. Six isolates of P. aeruginosae gave positive results and two yielded negative results, compared to all of the E. coli and K.pneumonia isolates (Figure 3 a,b&c).

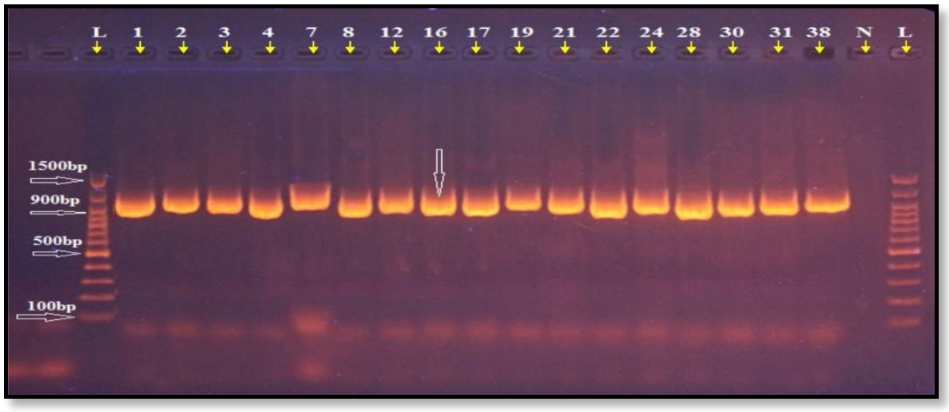

FIGURE 3 A: Gel electrophoresis for PCR product of (Escherichia coli primer) ,Lanes (1-38) represented positive results and Lane (N) represented Negative control .

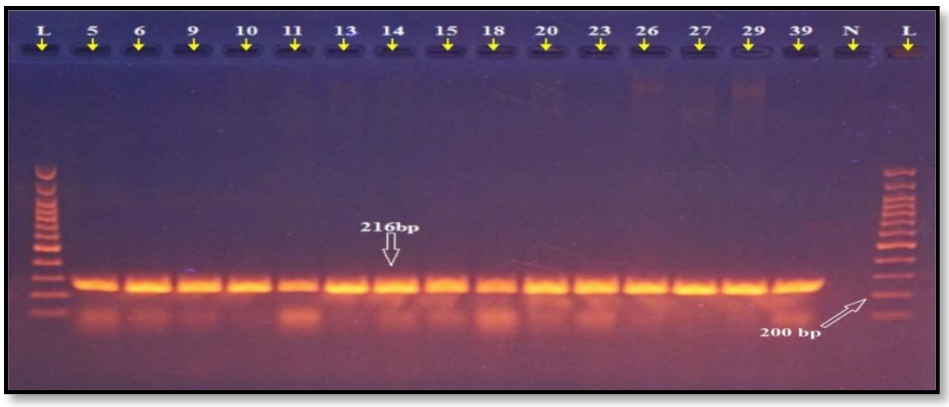

FIGURE 3 B. Gel electrophoresis for PCR product of (K. pnuemuniae primer, Lanes (5-39) represented positive results and Lane (N) represented Negative control .

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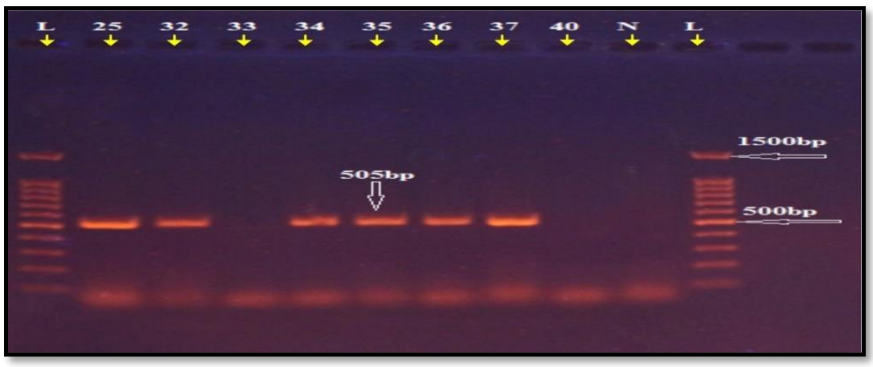

FIGURE 3C: Gel electrophoresis for PCR product of (P.aeruginosa primer) ,Lanes (25-35 and 34-37) represented positive results except lane (33 and 40) which represented Negative resulte and Lane (N) represented Negative control .

Genotype Screening of BlaSHV ,BlaIMP and Integron

The results for the blaSHV gene indicated its presence in 18 isolate(47.3%), (29.4%,27.27%,20%) respectively in E.coli with total percentage about (23.6%),(17.6%,27.27%,20%)respectively in K.pneumoniae and the total percentage about (18.4%)in all groups ; (17.6%, 9%, 0.0%) respectively in P.aeruginosa and totally was around (2%) (Figure 6 a &b) and (Table 6), as represented in the previous table there was high significant overall the groups P=0.001. The recent study pointed out that no bla IMP were detected in all isolates (Figure 7 a & b). In the present study, class1 integron was detected in(34)89.4% of all isolates in all groups ,E.coli ,K.pneumoniae and P.aeruginosae recorded (42.1% ,34.2%, 13.1%) respectively (Table 7) (Figure 8 a &b).

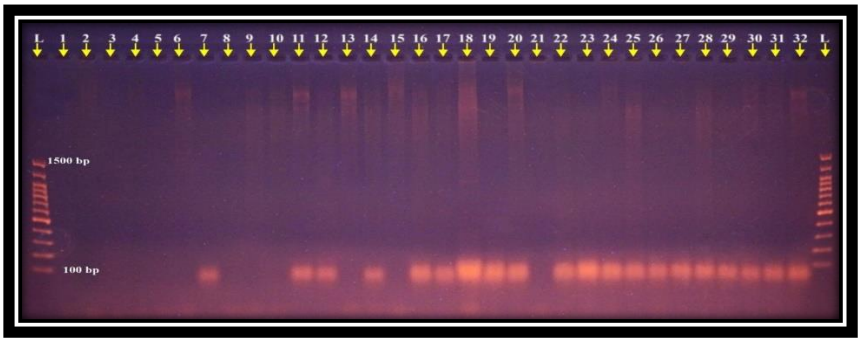

FIGURE 7 A: Gel electrophoresis for PCR product of (IMP primer) Lane (1-32) represented Negative result Lane (N) represented Negative control.

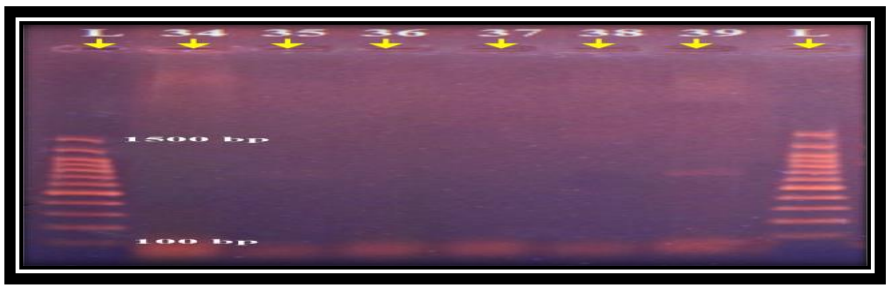

FIGURE 7 B: Gel electrophoresis for PCR product of (IMP primer), Lane (34-39) represented Negative result Lane (N) represented Negative control.

TABLE 6: Frequency of bla SHV gene in Bacterial isolates from all groups

PCR bla SHV Results %		Positive %	Negative %	Total No. & %
Group I	E. coli	29.4	17.6	18 (47.3)
	K. pneumonia	17.6	29.4	
	P. aeruginosa	0.00	17.6	E. coli 26.3% K. pneumonia 18.4% P. aeruginosa 2.0%
Group II	E. coli	27.27	18.18	
	K. pneumonia	27.27	9.0	
	P. aeruginosa	9.0	9.0	
Group III	E. coli	20.0	20.0	
	K. pneumonia	20.0	20.0	
	P. aeruginosa	0.00	20.0	
p. value for E. coli				0.503NS
p. value for K. pneumonia				0.004**
p. value for P. aeruginosa				< 0.001**
Overall p. value				0.001**

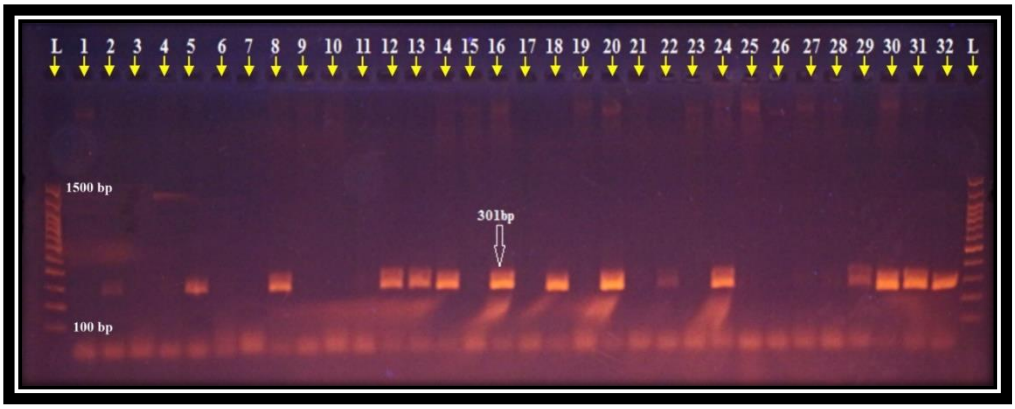

FIGURE 6 A: Gel electrophoresis for PCR product of (SHV primer), Lanes (2,5,8,12-14 ,16,18,20,22,24 and 29-32) represented positive results,Lanes (1,3,4,6,7,9-11,15,17, 19,21,23 and 25-28) represented Negative result Lane (N) represented Negative control .

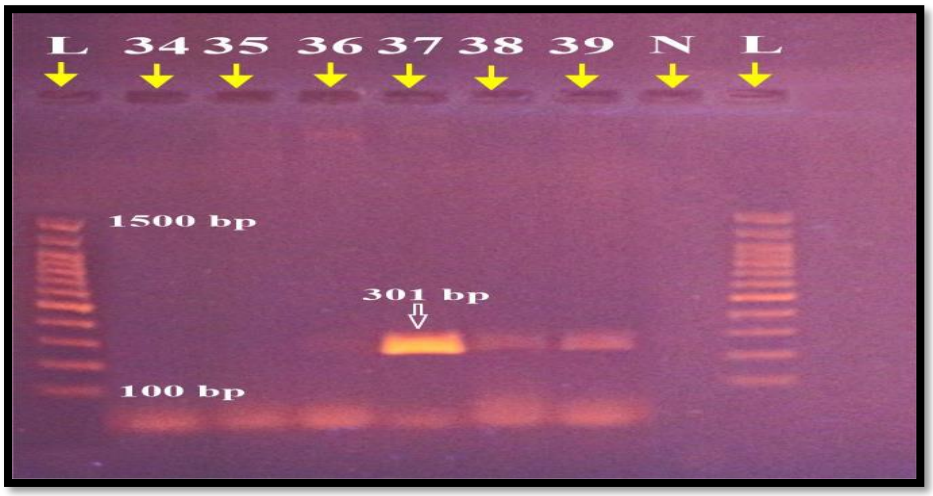

FIGURE 6 B: Gel electrophoresis for PCR product of (SHV primer) , Lanes (37-39) represented positive results,Lanes (34-36) represented Negative result Lane (N) represented Negative control .

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TABLE 7: Frequency of Int1 gene in Bacterial isolates from all groups

PCR Int I Results %		Positive %	Negative %	Total No. & %
Group I	E. coli	47.0	0.00	34 (89.4)
	K. pneumonia	35.2	5.8	
	P. aeruginosa	11.7	0.00	E. coli 42.1% K. pneumonia 34.2% P. aeruginosa 13.1%
Group II	E. coli	45.45	0.00	
	K. pneumonia	27.27	9.0	
	P. aeruginosa	9.0	9.0	
Group III	E. coli	30.0	10.0	
	K. pneumonia	40.0	00.0	
	P. aeruginosa	20.0	00.0	
p. value for E. coli				< 0.001**
p. value for K. pneumonia				0.005**
p. value for P. aeruginosa				< 0.001**
Overall p. value				0.024*

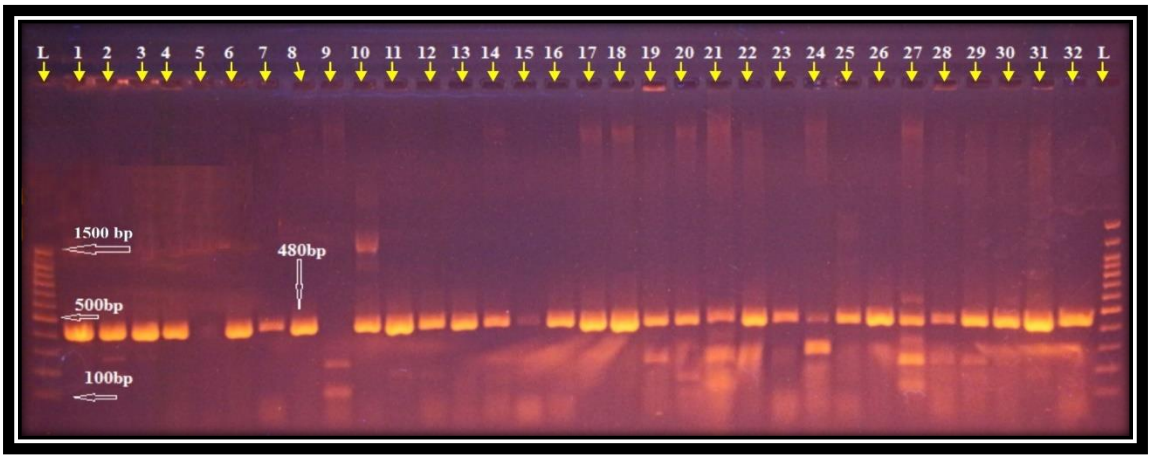

FIGURE 8A: Gel electrophoresis for PCR product of (Int 1primer), Lanes (1-4,6-8 and 10-32) represented positive results,Lanes (5 and 9) represented Negative result Lane (N) represented Negative control .

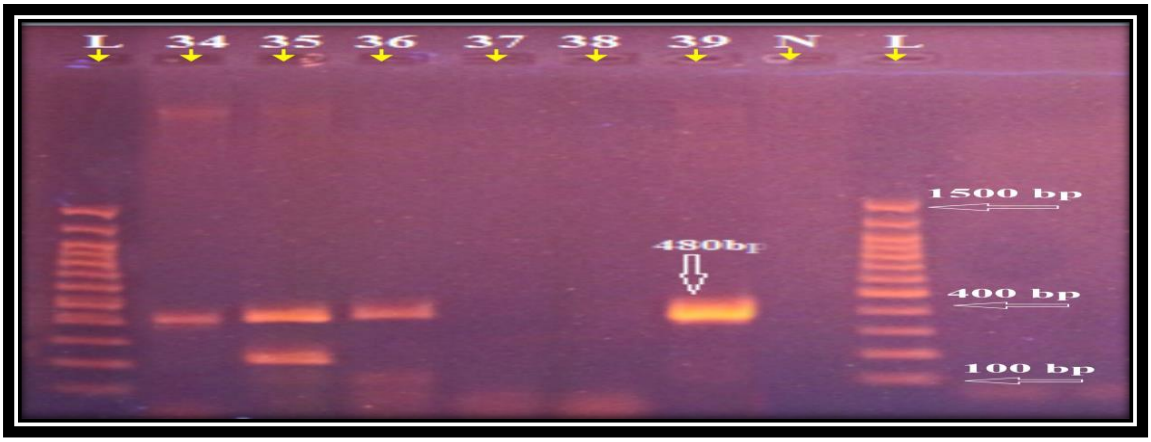

FIGURE 8 B: Gel electrophoresis for PCR product of (Int 1primer), Lanes (34-36 and 39) represented positive results,Lanes (37 and 38) represented Negative result Lane (N) represented Negative control .

DISCUSSION

Urinary tract infection (UTI) is one of the main causes of fever and morbidity in immune-compromised cancer patients. Atypical presentations are common in these patients, hence it's crucial to screen for UTI (23). The isolation rate from 200 patients in the recent study was as follows: 33 (33%) from patients with bladder cancer treated with BCG (Group-I), 23 (23%) from patients with bladder cancer treated with mitomycin C (Group-II), and 17 (42.5%) from control patients (patients with UTI but no bladder cancer) (Group-III). Our findings concur with those of (24), who reported that 73 (24%) of the 308 urine samples from cancer patients in Nebal that had been subjected to culture contained bacterial growth. (25) similarly in line with our findings, discovered that from approximately 199 bladder ca. patients in Mexico City, 20 patients (10%) had UTI following TURBT; 100 of the 497 processed samples from cancer patients in India who were thought to have UTIs tested positive for bacterial growth, according to (23); At Al-Diwaniya Teaching Hospital/Al-Diwaniya Governorate/Iraq, 33 urine samples from bladder Ca. were examined by(26), They identified (73%) of the uropathogens isolated from those samples. In our findings E. coli 13(13%), 9(9%), and 4(10%) were the most prevalent bacteria in Groups I, II, and III, respectively. These were followed by K. pneumonia 11(11%), 9(9%), and 4(10%), P. aeruginosa 5(5%), 3(3%), and 2(2%), and S. aureus 4(4%), 2(2%), and 1(2.5%) Other kinds in Group-III include Enterobacter cloacae 1 (2.5%), P. mirabilis 1 (2.4%), and M. morgani 4 (4%). The study findings were somewhat similar to those reported by Sime et al. in 2020, who stated that among the 292 urine samples from cancer patients in Ethiopia, E. coli was the most often identified uropathogen, followed by K. pneumoniae and Citrobacter diversus;Other Study conducted by (27) also agree with our current findings , they collected Urine samples from cancer patients in Pakistan and revealed that E. coli was the most prevalent followed by Klebsiella spp, S. aureus while 3 (7.1%) were Proteus spp and Pseudomonas spp.; In a Study conducted in Al- Nasiryah city by (28) also convergent with our findings ,they reported that only 90 samples from 330 urine give positive growth results and 57(63.3%) E.coli and 21 (23.3%) K.pneumoniae and 12(13.3%) From other Gram negative bacteria ; (29) reported that K. pneumoniae (31.2%), S. aureus (6.3%), Ps. aeruginosa, P. mirabilis, Enterococcus spp. (3.7% each), S. saprophyticus (2.6%), and Citrobacter spp. (0.4%) were the most common pathogens found in Najaf city specimens cultures , UPEC was found in 41.3% (111/269) of those specimens. According to Bhat et al., 2021, which contradicts our findings, the most prevalent isolates from cancer patients were Klebsiella spp. (18.30%), Pseudomonas spp. (17.65%), and E. coli (14.71%), followed by S. aureus (13.72%). Bla SHV in our findings was around 18(47.3%) from total isolates ,several previous studies in compatible with our results , in a study conducted for Clinical Isolates of Enterobacteriaceae in Sudan by(30) , they revealed that 44% of the isolates produced bla SHV gene ; another study similar in some extent to our findings including : (31), in which SHV (43.1%) ; other study which conducted in Gaza by(32),they reported that 38.3% of Enterobacteriaceae isolates were harbored bla SHV gene ; (33) incompatible with our findings ,they summarized that much lower percentage than our findings around 5.1% .

The recent study reported that blaSHV from all E.coli isolates about 26.3% and (29.4%,27.27,20%) in all groups respectively , this is in agreement with a study conducted in Erbil City, Iraqi Kurdistan Region by (34),they reported the presence of blaSHV in about (28.5%) of E.coli isolates ; Another study supported our findings was done by (32) investigated that around 20.6% of E. coli isolates had blaSHV; Additionally, (35)revealed that the rate of blaSHV around 20% ; The rate of blaSHV in this study was higher than that reported by (36) in an Iranian hospital (5.5%) which were E. coli isolates.

The frequency of blaSHV from all K.pnemoniae isolates about 18.4% and (17.6%,27.27%,20%) respectively in all groups ,this is in accordance with (37) ; in a study conducted in Iran ,they investigated that 15% of K.pnemoniae isolates harbored blaSHV gene ; (38)reported that the

prevalence of this gene in K.pnemoniae isolates in a Saudi Arabian tertiary hospital was about 23% ; (39) in a study conducted in a Turkish hospital ,the percentage of blaSHV was around (24.2%) all of which were K. pneumoniae isolates; our finding was much lower than that reported by (40) in a study carried out in Al Anbar city ,Iraq ,they investigated that the occurrence of blaSHV in K.pnemoniae isolates about 56.25%.The occurrence of blaSHV in P.aeruginosa isolates about 2 % and (17.6%, 9%, 0.0%) respectively in all groups ,this is similar in some extent with the result recorded by(41),they reported that the frequency of the blaSHV gene was 13.3% ; (42) revealed that 10.52% of P.aeruginosa isolates was carry blaSHV gene ; other study in Iran by (43) where the frequency of blaSHV gene was 6.6% ; (44) disagree with our findings ,they reported very high frequency for blaSHV in P.aeruginosa isolates about 86.66% .

The recent finding which regarding the absence of blaIMP from all isolates was sharing with multiple studies including : A study from Saudi Arabia and the Gulf countries conducted by (45) revealed that None of the E.coli isolates produced KPC or VIM or IMP ;(46) in a study conducted in Iran ,they investigated that no blaIMP and blaVIM genes were detected in E.coli isolates ; (47) in a study on E .coli isolates investigated that these isolates carry about 47.6% of blaIMP gene .Additionally (48) also detected that no blaIMP and blaVIM genes were found in K.pneumoniae isolates in a research conducted in Brazil ; (49) in a study conducted in Eygpt revealed that non from K.pneumoniae isolates were carry blaIMP gene ; (50) recorded that the frequency of bla IMP gene in K. pneumoniae isolates was 100 % in Zanjan .On the other hand (51) and other study conducted in Al –Nassiryah city, Iraq , (52),they revealed that non isolates of P.aeruginosa were carry the blaIMP , blaGIM genes ; (53)also disagree with the recent outcomes ,they reported that blaVIM and blaIMP were about 85% ,57% respectively .

Our study revealed that 34 (89.4%) of all isolates from all groups carried the class 1 integron gene , these results are consistent in some extent with those of (54),they reported that 73% of Gram nagetive bacteria were carry the class 1 integron gene ;(55) they revealed that Integrons were identified in 93% from all the studied strains ; while low percentage investigated by (56) they found that the prevalence rate of class I integron in their study was 54.2%.

E.coil isolates in the recent study were carry about 42.1% of class I integron gene and this finding compatible with that found by (57) reported that 37% of E coli isolates were have class I integron gene ;(58)they recorded that E. coli isolates were harbor class I integron gene in about 44.77% ; (59) recorded percentage little high than our ,they investigated that this gene present in about 59.5% of all E.coli isolates ; Abbas ,2015 disagree with our study ,he reported that only 4.5% of E.coli isolates were carry the class I integron gene. The frequency of Class I integron gene in K. pneumoniae isolates was 34.1% that was consistent with the studies of (60) with 36.6% frequency; (61) reporting 25.8% Class 1 integron in isolates; (62) reported that 28.6% of K. pneumonia isolates were carry Class I integron gene ; In another study reported by (61) the frequency of Class I integron gene was 74 % that is different from our findings . P.aeruginosae isolates carry Class 1 integron in about 13.1% in the recent study ,this finding were consistent to those recorded by (63) she reported that 16% of isolates carry this gene ; (64) invetigated that 12.4 % of P.aeruginosae isolates were harbor Class 1 integron ; (65) disagree with our results ,they found that 55.5% of P.aeruginosae isolates carry Class 1 integron.

CONCLUSION

The present study highlights a relatively higher prevalence of BlaSHV gene in Escherichia coli followed by Klebsiella pneumoniae and Pseudomonas aeruginosae .In view of these findings, we recommend the establishment of national guideline for the screening of ESBL in Cancer Patients . The strict compliance to antibiotic stewardship and enforcement of infection control practices should also be strengthened in all our Iraqi health centers. High prevalence of integron class 1 may be act as reservoir of antibiotic-resistant genes that has a

significant risk for spread of antibiotic resistance to pathogenic or commensal bacteria in the community.

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