Case Report

Antimicrobial Susceptibility Profile of Bacteria Isolated From Male Cancer Patients

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Abstract

Background : Cancer is the succeeding cause for deaths all inclusive, demonstrating an estimated

9.6 million Deaths. Urinary tract disease is a genuine medical issue in the network and medicinal services settings. The chances of creating infections are high in patients of cancer. Among those infections, urinary tract infections appear to be extremely normal. Pathogens that lead to UTI in malignant growth patients include E. coli, Proteus, Candida and Klebsiella. If untreated, UTI can lead to serious complications in men. Methods: Urine samples of male cancer patients were taken from the different hospitals of Lahore. Urine samples were plated on CLED media. Then identification of microorganisms was done by using gram staining and other biochemical testing while some were identified by using API kit. Results: Results showed that Escherichia coli was the most common and the most recurrently occurring uro-pathogen which means that Escherichia coli is the principal agent which causes urinary tract infection in the patients of cancer. While other pathogens that were found to cause urinary tract infection were K. pneumonia, P. aeruginosa, Staphylococci, Proteus spp. Then the sensitivity and resistance pattern of these uro- pathogens against different antibiotics were also checked. Physical and biochemical parameters were also high in male cancer patients. Conclusion: UTI affect all age groups. The high level of glucose in the urine promotes the growth of pathogens that leads to UTI in male cancer patients. While the frequent usage of antibiotics and broad spectrum antibiotics may cause the productionof antibiotic resistant pathogens in urinary tract. We can prevent UTI by controlling the factors which are responsible for increasing the risk of UTI in males.

Keywords: Cancer; Urinary Tract Infection; Resistance; Sensitivity; Antibiotics

Introduction

Cancer is an enormous gathering of infections which may begin in practically any body part or body tissue when unusual cells develop wildly, go past their typical limits to violence connecting regions of body as well as extent to various tissues. Cancer is a leading cause of death all over the world, demonstrating an estimated 9.6 million passing's in year 2018. Nearby, around 1 of all 6 deaths is for the reason of cancer [1]. There are many risk factors that are responsible for cancer, of which age, obesity and familial history are very important risk factors. As indicated by the modern measurable evidence from NCI's surveillance, epidemiology, and end result programs, the average age of cancer analysis is sixty six years. This denotes 50% cancer cases occur in persons under this age and other half in persons above that age. 1/4 of new cancer cases are examined in persons matured 65 to 74years [2]. The chances of creating Urinary tract infections are high in patients of cancer. Skin diseases, skin rashes, pneumonia (infection in lungs), infection in tissues and urinary tract diseases are normal in patients of malignant growth which can prompt genuine result. Among every one of these diseases, urinary tract infections appear to be extremely normal. Pathogens that lead to UTI in malignant growth patients incorporate Escherichia coli, Proteus, Candida and Klebsiella [3].

UTIs are getting continuously challenging to cure owing to no matter how you look at it ascent of an assortment of counter-agent poison restriction mechanisms. Of explicit concern are organisms from the family Enterobacteriaceae with E. coli as well as K. pneumoniae, which have both obtained plasmids encoding Extended Spectrum β-lactamases (ESBLs). This type of plasmids immediately spread insurance from 3rd-generation cephalosporins similarly as other antibiotics. Other members of Enterobacteriaceae yield the grade C β-lactamases that are dynamic against cephamycin despite 3rd-generation cephalosporins and moreover these are impenetrable to β-lactamase inhibitors. The presentation of AmpC proteins is also linked with carbapenem-resistance in K. pneumoniae strains missing the mark on a forty two kilo Dalton outer membrane proteins [4]. New antibacterial therapies that are impenetrable to inactivation via ESBL are being taken a shot at for usage in blend by novel modules of β-lactamase inhibitors that will target to both β- lactamases and K. pneumoniae carbapenemases. These

blend medicines have showed to be convincing in-vitro in contradiction of carbapenem-safe people from the Enterobacteriaceae family. Thusly, it's critical to recognize which against microbial instruments are accessible to a definite uropathogen in order to choose a practical cure [5].

Materials and Methods
Ethical Approval
The research work was approved by Departmental Research Ethics and Biosafety committee with reference no. D/2298/MMG.

Patient's Recruitment
The male patients for research were nominated from different hospitals like Mayo and Jinnah hospital, Lahore. All the agreed individuals were collectively 200 in number. Then all the people enlisted in study were isolated into two assemblies.
Group1: Normal healthy group (N=100)
Group2: Male cancer patients group (N=100)
Then all the physical and biochemical parameters were noted of healthy as well as cancer patients of different hospitals of Lahore. We used same selection criteria for selection of both healthy as well as cancer males group.

Collection and transportation of samples
Inspecting was done at the Mayo Hospital, Lahore. Just the willing patients were enlisted for the examination. Urine tests were gathered in dry, sanitized and sealed plastic bottles. Test samples were immediately moved to research center where they were plated on CLED media for further analysis.

Microscopy
One drop of pee was taken on glass slide and its smear was made. At that point the spread slip was determined to the smear and afterward it was seen under magnifying instrument.

Plating of Urine Sample on CLED Media
CLED media was arranged and afterward autoclaved. It was cooled then poured in the petri plates. 500 ul urine samples were plated on these petri plates. Petri plates were put on hatching brooded at 37°C for around 24 hours. After hatching, morphology of very much confined settlements was noted and absolute provinces' number was tallied. At that point isolated colonies of microbes were streaked on N-agar plates. After that bacterial strains were recognized by different biochemical tests.

Identification of microscopic organisms Biochemical Tests
Different biochemical tests like gram staining, Catalase, DNase, Oxidase, Motility, Indole, Urease, Methyl Red, Voges Proskauer, Citrate Utilization, Triple Sugar Iron were done for identification and characterization of isolated bacterial strains.

Antimicrobial Sensitivity Test
Mueller Hinton agar was arranged and autoclaved. Media was poured in petri plates. By utilizing q-tip settlement was streaked on plate. Diverse antibacterial circles were put on the plate. Plates were put on incubation at 37°C for 24. After incubation, zones of inhibition were recorded in mm

Estimation of Physical and Biochemical Parameters:
Physical parameters including age, weight, tallness and weight list (BMI) was determined. The biochemical boundaries which we evaluated incorporate sugar, HbA1c, cholesterol, LDL, VLDL, HDL, triglycerides, ALT, ALP, uric acid, creatinine and bilirubin. Both types of parameters were noted for both groups (control and cancer male group).

Statistical Analysis
All the physical and biochemical parameters of healthy group and caner patient's group were documented. After the data was arranged then "1-sample T-test" was applied with SPSS (version22) and found the mean values and standard errors in it. Resulted co-relations showed the significant difference in parameters with ($p \leq 0.05$).
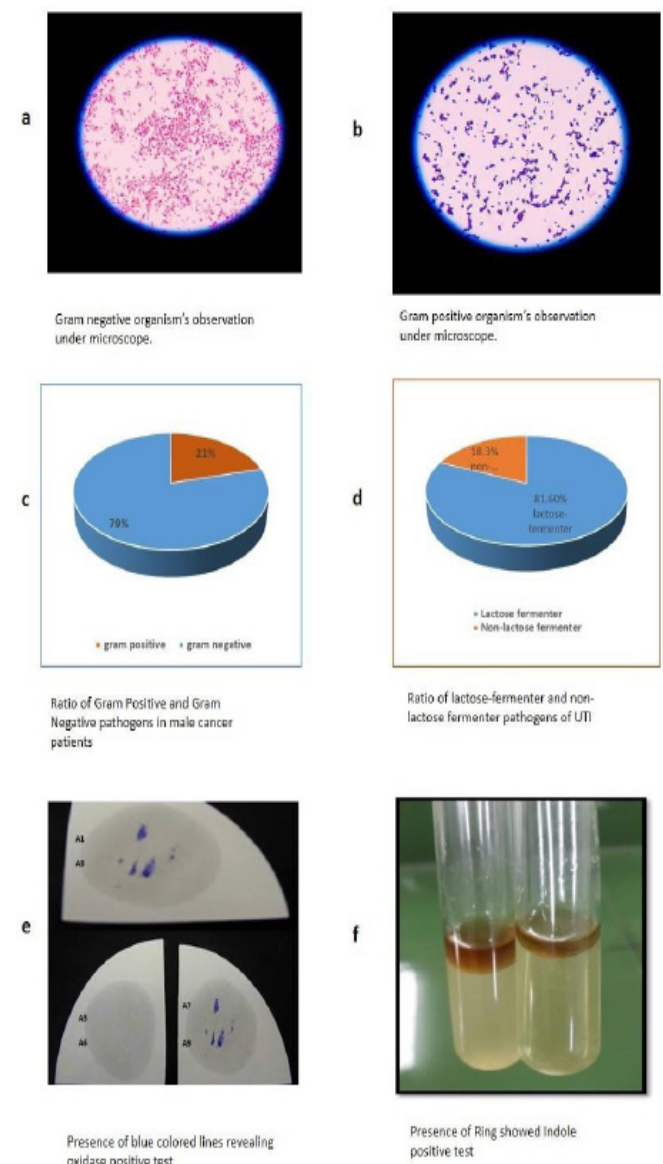
Results
Ethical Approval
The research work was approved by Departmental Research Ethics and Biosafety committee with reference no. D/2298/MMG.

Microscopy
Samples were taken from Jinnah Hospital, Lahore were 100 collectively. Then I took three strains from each plate that's mean total number of strains were 300. Pink and purple colored colonies of gram negative and gram positive bacteria respectively were shown in figure 1a and 1b (Figure 1a,1b). Percentages of different pathogens in UTI are shown in figure 1c (Figure 1c). It was observed that 79% pathogens were gram negative bacteria in males.

Culture results
As the UTI caused by lactose fermenter and non-lactose fermenter so we were observed that lactose fermenter was greater in percentage than non-lactose fermenter among UTI infections in cancer patients as shown in figure 1d (Figure 1d).

a. Gram negative organism's observation under microscope.

b. Gram positive organism's observation under microscope.

c. Ratio of Gram Positive and Gram Negative pathogens in male cancer patients

d. Ratio of lactose-fermenter and non-lactose fermenter pathogens of UTI

e. Presence of blue colored lines revealing oxidase positive test

f. Presence of Ring showed Indole positive test

**Results of Biochemical Tests for different pathogens**

All the biochemical testing was performed for the purpose of identification and further characterization of different types of gram positive and gram negative organisms. Results of all biochemical tests for further identification of gram negative microorganisms were summarized in table 1 (Table 1). Results of different biochemical tests like oxidase positive was shown in figure 1e and Indole positive test was shown in figure 1f (Figure 1e,1f).
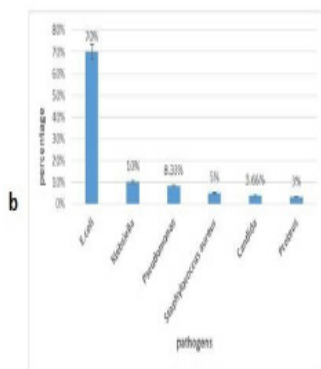
API (Analytical Profile Index) -20E

In API kit the slot of ONPG, IND, URE, TDA, LDC showed

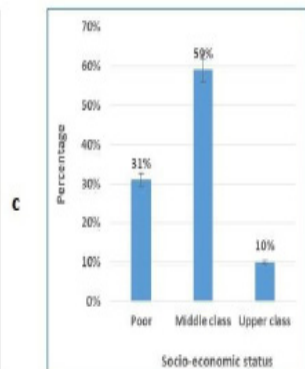**Table 1:** *Biochemical Reaction results of different pathogens*

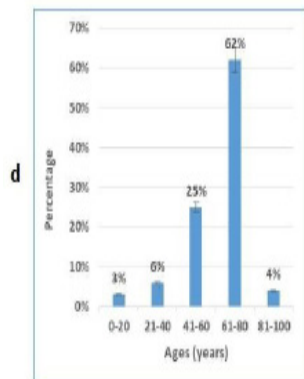| Organisms	Oxidase test	Citrate test	Motility test	Indole test	Urease test	slope	Butt	H2S	Gas
E.coli	-	-	+	+	-	Y	Y	-	+
Klebsiella	-	+	-	-	+	Y	Y	-	+
Proteus	-	+	+	-	+	R	Y	+	+
Pseudomonas	+	+	+	-	D	R	R	-	-
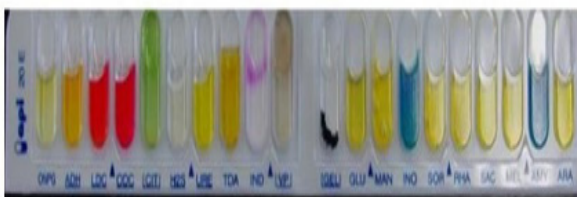
a   Results of API kit containing different biochemical reactions
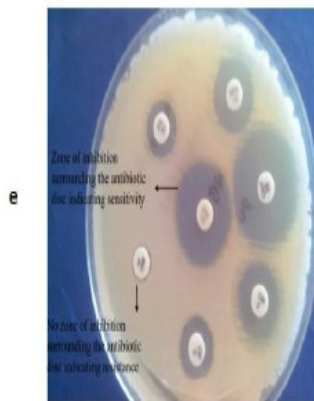

b   Frequency of UTI pathogens in male cancer patients

c   Socio-economic status distribution of UTI

d   Percentage of Age-wise distribution of UTI in male cancer patients

e   Different zones of clearance around antibiotics disc

positive result while the slot of CIT, H2S, ADH, ODC and INO showed negative result as shown in figure 2a (Figure 2a).

Frequency of UTI pathogens in male cancer patients

Pathogens were found in different percentages in male cancer patients as shown in figure 2b (Figure 2b). As described by figure, E.coli was found in higher percentage (70%) as compared to other microorganisms.

Socio-economic status distribution of UTI among male cancer patients

Socio-economic UTI distribution percentages was higher among middle-class male patients and its frequency is lower in upper class status patients as shown in figure 2c (Figure 2c)

Age wise distribution of UTI among male cancer patients

UTI infections were mostly observed in the age group of 61-80 years old and its frequency was lowest among the patients having age group ranges 1-20 years old as shown in figure 2d (Figure 2d).

Antimicrobial susceptibility profile of different microorganisms

Different zones of inhibition were shown in figure 1e (Figure 1e). The zones of inhibition formed by different microorganisms against different antibiotics were noted in mm and summarized in table 2 (Table 2).

Table 2 showed the sensitivity profile of E.coli against different antibiotics. As shown by the table the E.coli was highly resistant towards cephalexin followed by cefixime, naladixic acid and somehow pipemidic acid. While this microorganism was sensitive towards ciprofloxacin, amoxicillin, imipenem,

Table 2: *Sensitivity pattern of certain microorganisms against different antibiotics.*

Sensitivity (zones of inhibition in mm)					
Antibiotic	E.coli.	Klebsiella	Pseudomonas	S. aureus	Proteus
Amoxicillin(AMC)	70	55.5	40.2	98	99
Ciprofloxacin (CIP)	87	69.5	91.1	0	100
Cephalexin (CL)	29.7	18.2	13.5	0	0
Imipenem (IMP)	96	98.5	74.9	99	99
Cefizox (ZOX)	79	96.8	70	100	100
Cefixime (CFM)	36.6	15.2	39	0	0
Naladixic Acid (NA)	37	21.9	37	0	0
Nitrofurantoin (F)	72	96.8	72	99	0
Pipemidic Acid (PIP)	61.3	23	62	0	0
Ceftazidime (CAZ)	66.4	66.7	65.3	0	99.8

cefizox, nitrofurantoin and ceftazidime. This means that these medications may be given to patients having UTI infection.

Klebsiella showed a great variation in sensitivity profile against different antibiotics as described in table 2 (Table 2). This figure showed that this microorganism was highly resistant to cephalexin followed by cefixime, amoxicillin, naladixic acid and pipemidic acid. While Klebsiella showed great sensitivity against ciprofloxacin, imipenem, cefizox, nitrofurantoin and ceftazidime. So we can give these antibiotics to UTI infected patients.

Pseudomonas have a different susceptibility pattern against mentioned antibiotics as shown in table2 (Table 2). This microorganism was resistant to amoxicillin followed by cephalexin,

cefixime and naladixic acid. While Klebsiella showed sensitivity towards ciprofloxacin, imipenem, cefizox, pipemidic acid, ceftazidime and nitrofurantoin. This means that these antibiotics can be administrated to UTI patients.

Different microorganisms shows different patterns of sensitivity and resistance against different antibiotics. Staphylococcus aureus showed susceptibility patterns against used antibiotics asdescribed by table 2 (Table 2). This microorganism showed resistance to ciprofloxacin followed by cephalexin, cefixime, naladixic acid, pipemidic acid and ceftazidime. While this organism was highly sensitive against amoxicillin, imipenem, cefizox and nitrofurantoin. This means that these antibiotics may be given to patients suffering from UTI infection.

Sensitivity pattern of proteus against different antibiotics showed that proteus was highly resistant towards cephalexin followed by cefixime, naladixic acid, nitrofurantoin and pipemidic acid while this microorganism showed a great sensitivity against amoxicillin, ciprofloxacin, imipenem and cefizox. This interpret that these medications may be given to UTI infected patients.

Statistical Analysis
Study Groups
All individuals recruited in study were divided into two groups.
Group1: Normal healthy control group
Group2: Cancer patients group
Assesment of Physical Parameters:
The parameters of physical assessment of normal male individuals and patients suffering from cancer were taken from Mayo Hospital Lahore. All the results were described in table 3 (Table 3). These parameters were:
Age (Years)
Age were noted in terms of year. The mean ages of healthy controls subject calculated as 44.6±1.57 years while the mean of age of male patients suffering from cancer calculated as 62.02±2.4 years. The difference in the mean ages of both categories was statistically noteworthy (P<0.001)*.
Height (m)
The mean height of the normal healthy subjects was

Table 3: *Physical and biochemical parameters of control and cancer patients (male).*

Physical parameter	Control (N=100)	Male cancer (N=100)
Age	44.6±1.57	62.02±2.42
Height (m)	1.6003±0.009	1.6102±0.065
Weight (kg)	59.3±0.793	71.68±2.1
BMI (kg/m2)	24.9±0.38	28.42±0.8
Biochemical parameters		
Blood Fasting Sugar (mg/dL)	96.3±2.99	203.2±10.67
Bilirubin (mg/dL)	0.352±0.007	0.763±0.018
Creatinine (mg/dL)	0.90±0.012	0.9±0.017
Uric acid (mg/dL)	13.7±0.09	13.9±0.17
HbA1c (%)	5.39±0.27	9.90±0.92
Cholesterol (mg/dL)	156±2.78	158.1±4.12
LDL (mg/dL)	95.08±2.15	105.4±3.82
VLDL (mg/dL)	17±1.24	32.4±2.32
HDL (mg/dL)	44.48±0.62	46.6±0.74
Triglycerides (mg/dL)	141.24±9.63	232.9± 21.28
ALT (U/L)	31.7±2.0	43.9±5.5
ALP (U/L)	109.02±1.25	203.9±9.00

1.6003±0.009 meters while the mean height of men having cancer was 1.6102±0.065 meters. The difference in the mean height of both groups was statistically noteworthy (P<0.001).
Weight (kg)
Mean weight of the healthy controls was 59.3±0.79kg and the mean weight of the men having cancer was 71.68±2.1 kg. The differences in the mean weight of above groups was highly noteworthy (P<0.001)*.
BMI (kg/m2)
The mean BMI of the normal healthy subject was 24.9±0.38 kg\m2, while the mean BMI of the patients having cancers calculated as 28.42±0.8 kg\m2. The differences in the mean BMI of both categories was highly noteworthy (P<0.001)*.

Assessment of Biochemical Parameters
Blood Sugar Fasting:
The mean blood sugar fasting of the normal control subjects was 96.3±2.99 mg\dL, while the mean blood sugar fasting of the patients having cancer was 203.2±10.67 mg\dL. The difference in the mean blood fasting sugar of both groups was statistically important (P<0.001)*.
Bilirubin (mg/dL)
The mean bilirubin of normal healthy subjects was 0.352±0.007 mg\dL while the mean bilirubin of the patients with cancer was 0.763±0.018 mg/dL. The difference in the mean bilirubin of both groups was statistically highly important (P<0.001)*.
Creatinine (mg/dL)
The mean creatinine of the normal healthy control subject was 0.90±0.012mg\dL while the mean creatinine of the patients with cancer was 0.9±0.017. The difference in the mean creatinine of both study groups was not statistically important (P>0.05).
Uric Acid (mg/dL)
The mean uric acid of the normal healthy control subject was 13.7±0.09 mg\dL while the mean uric acid of the patients having was 13.9±0.17. The difference in the mean uric acid of study groups was statistically highly noteworthy (P<0.001)*.
HbA1c (%)
The mean HbA1c of the normal healthy control subject was 5.39±0.27%, while the mean HbA1c of the patients with cancer was 9.90±0.92%. The difference in the mean HbA1c of both study groups was statistically significant (P<0.001)*.
Cholesterol (mg/dL)
The mean cholesterol of the normal healthy subjects was 156±2.78mg\dL while the mean cholesterol of the patients suffering from cancer was 158.1±4.12. The difference in the mean total cholesterol in both groups was not statistically significant (P>0.05).
LDL (mg/dL)
The mean LDL of the healthy subjects was 95.08±2.15mg\dL while the mean LDL of the patients having cancer was 105.4±3.82 mg/dL. The differences in the mean total LDL in both groups was not statistically noteworthy (P>0.05).
VLDL (mg/dL)
The mean VLDL of the healthy subjects was 17±1.24 mg\dL while the mean VLDL of the patients with malady was 32.4±2.32 mg/dL. The difference in the mean total VLDL was statistically highly significant in both groups (P<0.001)*.
HDL (mg/dL)
The mean HDL of the normal controls subject was 44.48±0.62 mg\dL while the mean HDL of the patients having cancer was 46.6±0.74 mg/dL. The differences in the mean total HDL of both groups was statistically highly important (P<0.001)*.

Triglycerides (mg/dL)

The mean triglycerides of the healthy control subject was 141.244±9.63 mg\dL while the mean triglycerides of the patients with cancer was 232.9±21.28 mg/dL. The differences in means total triglycerides among both groups was statistically highly notable (P<0.001)*.

ALT (U/L)

The mean ALT of the normal healthy control subject was 31.7±2.0 mg\dL but the mean ALT of the patients suffering from cancer was 43.9±5.5 mg/dL. The differences in the mean total ALT in both groups was statistically highly important (P<0.001)*.

ALP (U/L)

The mean ALP of the normal healthy subject was 109.02±1.25 mg\dL while the mean ALP of the patients suffering from cancer was 203.9±9.00 mg/dL. The differences in the mean total ALP in both categories was statistically highly noteworthy (P<0.001)*.

Discussion

Cancer growth is a social event of ailments incorporating uncommon cell improvement with the likelihood to assault or extent to various bits of the body. These show up contrastingly comparable to liberal tumors, which don't spread. Likely signs are join a bulge, unusual kicking the bucket and deferred hack, lessen weight, and an alteration in strong releases. While these reactions may show infection and become the reasons of cancers. Almost hundred types of cancers impact individuals [6]. Tobacco usage is the main reason behind about 22% of dangerous development passings. Another 10% are a result of weight, not exactly heavenly eating everyday practice, nonappearance of physical activity or over-drinking of alcohol [7]. Various constituents fuse certain ailments, radiation interaction and characteristic toxic substances. In the making scene, 15% of tumors are a direct result of pollutions, for instance, Helicobacter pylori, hepatitis B/C, human papillomavirus illness, Epstein–Barr disease and HIV. These factors showing, in any occasion generally, by altering the characteristics of a cell. Normally, various innate changes are mandatory before danger makes. Nearly 5–10% of dangerous growths are a result of obtained inherited blemishes from a family people [8].

Dangerous development can be perceived by explicit signs and reactions or screening tests. It is then usually further explored by clinical imaging and attested by biopsy [9].

The bacterial etiology of urinary infections have been seen excessively settled and practically reliable. Escherichia coli consider as the extraordinary uropathogen (80%) separated in extreme system acquired straightforward sicknesses, trailed by Staphylococcus saprophyticus (10% to 15%). Klebsiella, Enterobacter, and Proteus species, and enterococci once in a while cause straightforward cystitis and pyelonephritis [10]. Our examination moreover revealed that E.coli is the most widely recognized pathogen followed by Klebsiella, Pseudomonas, staphylococcus, candida and proteus.

In an important examination, Gram-negative pathogens indicated a practically identical defenselessness example to the vast majority of the anti-toxins, while the Gram-positive Staphylococcus agalactiae showed totally various examples. For sure, the most predominant pathogen, E. coli, showed moderately higher antimicrobial obstruction rates against the vast majority of the tested anti-infection agents, that is, cephalothin (58%), trimethoprim- sulfamethoxazole (48%), ciprofloxacin and ampicillin/sulbactam (34%), cefotaxime (28%),ceftazidime (26%), amoxicillin/clavulanate (20%), nitrofurantoin (4%), and amikacin (2%). In like manner, Klebsiella pneumoniae indicated comparable examples of protection from trimethoprim- sulfamethoxazole (47%), ampicillin/sulbactam (42%), cephalothin (42%), ciprofloxacin (34%),cefotaxime (25%), amoxicillin/clavulanate (24%), ceftazidime (22%), nitrofurantoin (11%), and amikacin (2%), separately. Enterobacter species obstruction design was as per the following: cephalothin (40%), amoxicillin/clavulanate (32%), cefotaxime (32%), ciprofloxacin (24%), ampicillin/sulbactam (24%), and ceftazidime (20%), and just 4% of strains were impervious to amikacin [11].

The primary objective of treating UTI is to take out pathogens. So exploring the bacterial opposition and affectability is of most extreme significance.

It is inferred that Urinary tract disease is a genuine medical issue in the network. Malignant growth patients are at high danger of urinary contaminations because of disease chemotherapy prompts serious and delayed immunosuppression, for example, neutropenia during chemotherapy, modified gut greenery as a result of successive anti-infection organization, and interruption of skin and harm of epithelial surfaces of the tissues by cytotoxic chemotherapeutic operators. Because of this, it is a genuine medical issue that includes bacterial attack and increase in the organs of urinary tract framework. Visit utilization of anti-toxins may cause the creation of anti-microbial safe pathogens in urinary tract [12].

The mean of all the physical and biochemical parameters was higher in male disease patients when contrasted with solid control people. The assessment of these boundaries can help in early finding of a disease and malignant growth. Thus by controlling numerous variables an individual can forestall of having disease just as malignant growth.

Undertaking

It is undertaking that this research article has not published before and all authors are agreed to publish in this journal. The author(s) declare that the publication of this article has no conflict of interest.

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