URINARY TRACT INFECTIONS – ADVANCEMENT IN THE STRATEGIES

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Abstract

The infection occurring in any part of the urinary system is a urinary tract infection. It is limited to the lower urinary tract i.e., up to only the bladder and the urethra but, if it is not treated in early times the infection can spread to the kidneys causing a condition of pyelonephritis. This kidney infection can cause permanent kidney damage. This infection can occur at any age and to any gender, but it is more common in women than in men. It is because of the anatomical makeup of the former.

Various microbes are pathogenic and cause infection in the urinary tract but amongst them, the microorganism which is majorly seen as the notorious one is *Escherichia coli*. The bacteria attaches itself to the epithelial wall and overcome the flow of urine. This in a way helps them to remain in the tract and causes infection. The microbe internalizes itself into the cells which creates the chances of recurrent infection. To treat the infection antibiotics are a major help as they bring relief within three days. In recent times this treatment is now not as effective as it was earlier in the past few years. This condition has arrived due to the resistance towards the antibiotic-induced in the microorganism because of the exploitive use of antibiotics. Nowadays an effective approach is being taken which is known as Complementary and Alternative Medicine.

This alternative treatment consists of natural compounds such as the use of medicinal plants, dietary supplements, and probiotics used in treating the infection. This treatment is highly popular in USA-like countries because it only cures the infection but also helps in preventing it. There is a new way of treating and preventing the infection by producing vaccines that will train the bladder how to fight off the pathogenic microbe. It becomes easier to cure any disease if it is diagnosed at an early stage. It is the same in the case of UTIs where early detection plays a key role in treating the infection. Here comes artificial intelligence which is used in finding the early symptoms of urinary tract infections.

Keywords: Urinary tract Infection, Pathogens, Plants Nosocomial infections

Introduction

Urinary tract infections are infections that can occur at any time and in any area of the urinary tract, though it is limited to the lower section of the urinary system. Most commonly the bladder and the urethra are the affected ones, but the infection can spread to the kidneys which is a threatening situation. The condition is called pyelonephritis where the kidneys swell and cause permanent. Pyelonephritis occurs due to disruption in urine flow which can be due to any reason [1,12].

Pyelonephritis – An Extended Urinary Tract Infection

UTI begins with the entrance of bacteria in the bladder via the urethra where it increases in number and distributes to cause infection, from the bladder bacteria travel to the kidneys through the ureters. Later it causes severe kidney infection. This is known as acute pyelonephritis, but it can turn into a chronic infection. When there is repeated occurrence of this condition it is known as chronic pyelonephritis. It is more common in children than in adults. The presence of blood or pus in the urine can decide the infection [5].

Women are more susceptible than men to getting a Urinary Tract Infection

The infection can occur to anyone once in their lives, but it is seen that women are more prone to get the infection than men and it is recurrent in women most commonly. It is due to their anatomical structure where the bacteria travels from the anus to the bladder due to the shorter length of the urethra than men. The bacteria is present in our gastrointestinal tract from where it travels to the anus. Not only due to the anatomical structure being the only reason for any woman to get an UTI there are other reasons also. Pregnancy is one of the reasons for getting a UTI where due to hormonal changes there is a shift in microflora. This in turn makes the region more susceptible to attracting urinary tract infections. If the bladder is not emptied properly then with the leftover

urine also the infection can occur which is a situation in pregnancy where due to pressure of the uterus on the bladder it becomes difficult to cut the urine from the body [6].

Menopause is another major reason because during menopause there is a certain drop in the estrogen level which changes the physical nature of tissues present in the vagina as it becomes dry and thin. This change makes the growth of pathogenic bacteria hustle-free [6].

According to the statistics, 50-60% of women will get a UTI which is a very frequent infection to get which is up to 25-30% [7]. It is up to thirty times more frequent than men i.e., 38-40% for women and about 10-12% for men are the chances of getting a UTI. There are cases where women get the infection twice within 4-6 months, the rates show 40% of women are affected by this [7].
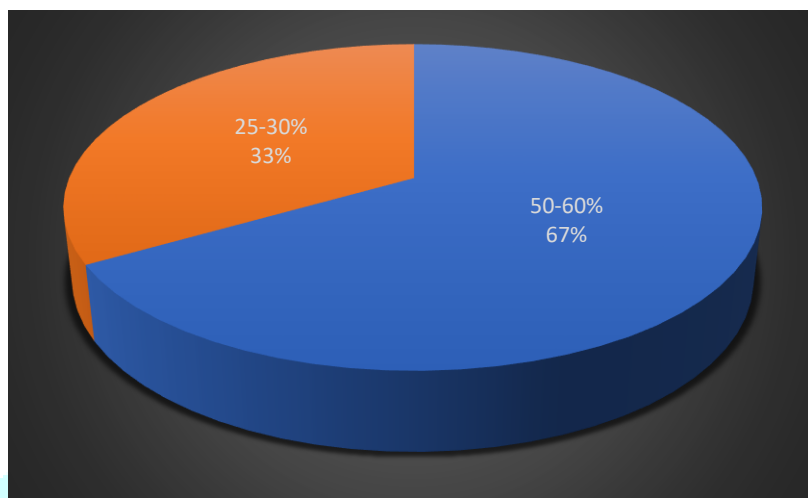

Figure 1

The microorganism responsible for the infection and its pathogenesis

Various microorganisms manage to cause infection. The microbes are *Proteus mirabilis*, *Staphylococcus saprophyticus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Escherichia coli,* and *Pseudomonas aeruginosa*. But among them, *E. coli* is the most notorious one. Is seen that from the urine sample detected that up to 90% of isolates were of this uropathogenic microbe. As this bacteria is present in our body, it becomes easy for the bacteria to travel from the anus to the urethra, where its multiplies itself into countless numbers and colonizes the bladder. There it acts as a pathogen [3].

These microbes have special features which help them to remain attached to the area. That feature is fimbriae which have a special adhesive power with which it attaches itself to glycolipids and glycoproteins present on the epithelial surfaces [3]. In this way, they prevent themselves from flowing away with the urine and remaining in the urinary tract. These microbes only cause recurrent infection by making the epithelial cells their reservoir. As the microorganism is capable of producing toxins that disintegrate the epithelial lining and enter the cells. Before living on the epithelial surface, it first reaches the outer region of the particular area like the perineum and periurethral and then the bacteria starts the infection.

Before causing the infection, these pathogenic microbes have to fight against the normal microbiota present in that region. As the microflora supplies us with an added defense by fighting and cutting the pathogen. *Lactobacillus*, *Staphylococcus epidermidis*, *Corynebacterium* [3].

Detection of microorganisms causing urinary tract infection

To detect the infection, the urine sample is collected in a small bottle. The bottle should be sterile and opened at the time of collecting the sample only. After receiving, the sample should be cultured on Cled Agar media and incubated for 24 hours at 32ºC to 35ºC. After the incubation period, pink-colored colonies were grown on the media plate. Then from the plate, a culture is picked up and stained under the gram stain procedure. The grain stain showed pink-colored colonies which detected the presence of gram-negative bacteria in the sample. After staining the colonies were detected for the catalase test. The test showed positive results. Hence, the microorganism was catalase positive. This test is known as the rapid test. After the rapid test, different biochemical tests were performed. The first test is indole test was performed similarly other tests were also performed which are the methyl red test, citrate test, urease test, mannitol salt test, and TSI test.

Biochemical Tests and their Interpretation

S.No.	Biochemical Test	Observation	Result
1	Indole Test	Red Color	Positive
2	Methyl Red Test	Red Color	Positive
3	Citrate Test	No Color Change	Negative
4	Urease Test	No Color Change	Negative
5	Mannitol Salt Agar	Stab line with the change in color from red to yellow	Positive
6	Triple Sugar Iron	Yellow Color	Positive

Table Number 1

After all these tests were performed it was confirmed that the pathogenic microorganism present in the urine sample is *Escherichia coli*. It was seen that the majority of the urine sample had this bacteria only. It shows that the people contracted UTI because of this microbe.

Artificial Intelligence – Latest Technique to Detect Urinary Tract Infection

Artificial Intelligence is opening a new pathway in the healthcare industry which helps in the early diagnosis of a disease. A comparable situation is with this infection also, where artificial intelligence detects the early symptoms of urinary tract infections. The technique used is non-negative matrix factorization which detects the marker which can originate the infection. The technique is combined with the machine which gets the algorithm into itself. This in turn creates a portal to find the symptoms of the infection. It not only detects the symptoms but also can acknowledge the danger of getting sepsis in patients with serious complications. Because in these patients there is an elevated risk where the bacteria can enter the blood [10].

The basic principle of AI is getting machine knowledge i.e., to learn algorithms and statistical models. As machine knowledge can clear out various difficulties which are associating two variables, classification of subjects on different parameters, predicting the result depending on certain criteria, and identification of objects following similar patterns. There are several types of machines which is based on the principle of machine knowledge, and these are as follows: -

1. Support Vector Machine (SVM)
2. Random Forest (RF)
3. Decision Tree (DT)
4. Artificial Neutral Network (ANN)

To evaluate the machines, routine examination data and diagnosis results of UTI patients were collected, and a UTI datasheet was made out of it. Then these four machines were made as a dummy to detect the result based on the datasheet prepared. Above all four ANN showed the most correct result from 96% to 98%. To use ANN as a proper diagnostic tool, a few modifications can be done by adding variables of pollakiuria, suprapubic pain, and erythrocyturia. As these changes act real and can be applied in the real world [9].

Antibiotic Resistance

The cure for any bacterial disease is by the use of antibiotics, they are considered great discoveries in health care. But due to exploited use of antibiotics the pathogenic bacteria are changing themselves and becoming resistant. Till a decade ago the UTI was easily treated by antibiotics, and the situation is reversed now. When the sample was evaluated with antibiotics it was seen that the maximum of the antibiotics were resistant. Twenty-three types of antibiotic discs were used in the disc diffusion method. Out of that, only nine showed sensitivity by forming a zone of inhibition.

Antibiotics Showing Positive and Negative Results

S.No.	Antibiotic	Observation	Result
1	Ampicillin	No zone of inhibition	Negative
2	Piperacillin	No zone of inhibition	Negative
3	Cefixime	No zone of inhibition	Negative
4	Cefotaxime	No zone of inhibition	Negative
5	Ampicillin/Sulbactam	No zone of inhibition	Negative
6	Ceftriaxone	No zone of inhibition	Negative
7	Cefipime	No zone of inhibition	Negative
8	Cefoxitin	No zone of inhibition	Negative
9	Pipracillin/Tazobactam	No zone of inhibition	Negative
10	Amoxycillin/Clavulanic	Zone of inhibition	Positive
11	Tobramycin	Zone of inhibition	Positive
12	Gentamycin	Zone of inhibition	Positive
13	Ciprofloxacin	Zone of inhibition	Positive
14	Levofloxacin	Zone of inhibition	Positive
15	Norfloxacin	No zone of inhibition	Negative
16	Co-Trimoxazole	No zone of inhibition	Negative
17	Tetracycline	Zone of inhibition	Positive
18	Aztreonam	No zone of inhibition	Negative
19	Imipenem	Zone of inhibition	Positive
20	Nitrofurantoin	Zone of inhibition	Positive
21	Polymyxin-B	Zone of inhibition	Positive
22	Ceftazidime	No zone of inhibition	Negative
23	Clavulanate	No zone of inhibition	Negative

Table Number 2

The above table shows the number and types of antibiotics used which interpreted the result according to the observation.
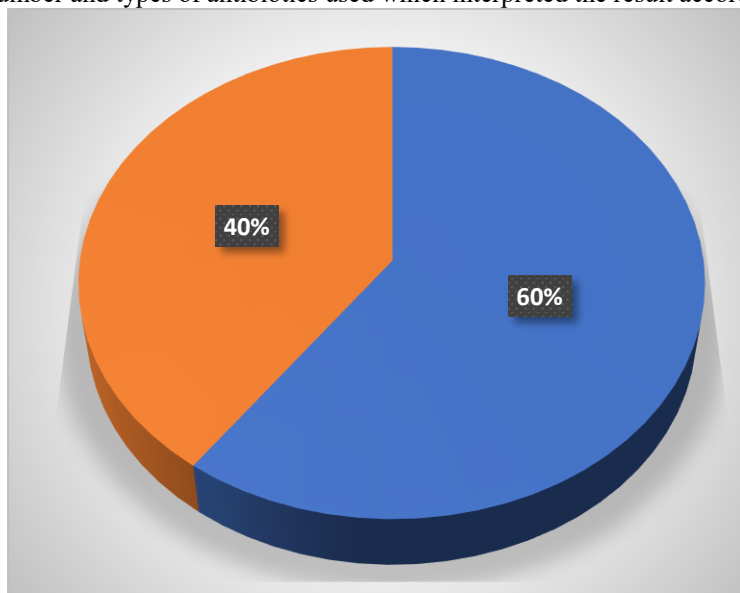

Figure Number 2

The figure shows only 40% of the antibiotics showed a positive result i.e., the zone of inhibition was seen in them only. The rest 60% were resistant in which zone of inhibition was not seen. The antibiotics which showed the sensitivity are as follows: -
 1. Amoxycillin/Clavulanic
 2. Tobramycin
 3. Gentamycin
 4. Ciprofloxacin
 5. Levofloxacin
 6. Tetracycline
 7. Imipenem
 8. Nitrofurantoin
[9]. Polymyxin-B

Study Conducted in the year 2013.
A study was done on multidrug-resistance *E. coli* which were isolated from hospitalized patients in Kolkata, India by Mandira Mukherjee, Shreya Basu, and Monalisa Majumder in the year 2013 where they worked on two hundred urine samples. They saw that 55% of isolates were of bacteriuria and within that 55% isolates 36% were of *E. coli* [2]. Later the bacterium's resistance to sixteen antibiotics was seen. The observation showed that NF (72.5%), and AK (70%) were found to be extremely sensitive. GEN (45%), LE (45%), and TOB (37.5%) also showed sensitivity. But most of them were resistant. AMP should highest resistance with 97.5%. The other antibiotics which showed resistance were NA (95%), CN (95%), AMX (92.5%), COT (82.5%), and CIP (65%). In the case of a third-generation cephalosporin, the result was CTX (67.5%), CTR (62.5%), and CAZ (17.5%). These antibiotics were found to be resistant. For the confirmation of ESBL, a test was performed in combination with CAC-CAZ along with CTX-CEC. It was seen that by 5mm there was an increase in the area of inhibition in CAC from the other three CAZ, CEC, and CTX, respectively. Along with among 18 ESBL producers seventeen were resisting various drugs [2].

There is an alternative way to treat the infection other than making use of antibiotics. It is known as Complementary and Alternative Medicine. This alternative treatment consists of natural compounds such as the use of medicinal plants, dietary supplements, and probiotics used in treating the infection. This treatment is highly popular in USA-like countries because it only cures the infection but also helps in preventing it. Alone CAN cannot help to cope with the urinary tract infection, antibiotic treatment should be companioned with this regime which can together bring effective results. Herbal medicines have played a significant role in treating various diseases because they tend to deduct bacterial resistance towards antibiotics. Also, plants have such chemical compounds which prevent them from the attack by pathogenic microbes. These all qualities can help the patients suffering from UTIs as they give a relieving effect and also prevent them from contracting [11].
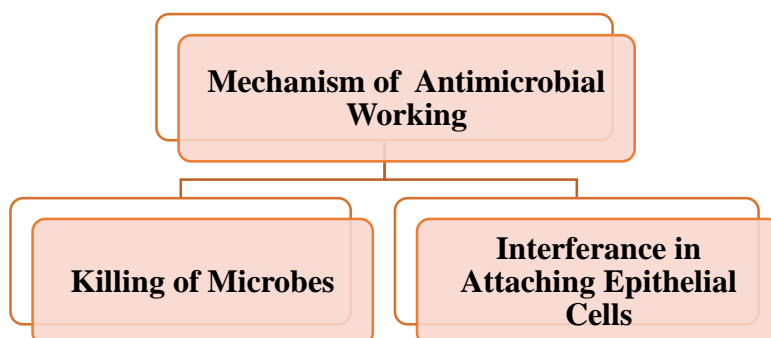
The figure shows how antimicrobial agents present in the plants work against the pathogenic microbe. In the first case, the agents kill the pathogen, so there are no chances of causing pathogenesis and in the second case it shows that if how the bacteria survive in that spot, then by interfering with the attaching mechanism of the microbe, it can be treated [11].

Medicinal Plants Used in Treating Urinary Tract Infections

There are diverse types of medicinal plants that can function as an antibiotic in fighting against the pathogen which is as follows: -

Bearberry (*Arctostaphylos uva-ursi*)

The effective part of this plant is the leaves which are used in diuretic properties. Due to this quality, the plant is also used in treating UTIs. So, the herb is widely used in the West to treat bladder infections and inhibit *Escherichia coli* from causing any infection [11]. It acts as an antimicrobial agent by carrying hydroquinone glucuronide to the kidneys and through it is excreted in the urine. There it is decomposed into hydroquinone function as an antimicrobial agent [11].

Figure 3 [13]

Juniper (*Juniperus communis*)

The effective part of this plant is terpenoids present in the leaves function as an antimicrobial and diuretic agent. The oils present in the plant are effective enough to treat Urinary Tract Infections [11]. This oil is known as terpinene-4-ol which is volatile. The leaves and berries are the main source of the oils. But this oil has some nephrotoxin compounds, they only act toxic if they are given in high doses [11].

Figure 4 [14]

Cranberry (*Vaccinium macrocarpon*)

The plant is effective against *Escherichia coli* which majority of the time causes UTI by preventing the attachment of the bacteria to the epidermal cells of the bladder. This in a way helps in inhibiting us from disease because if the microbe is not attached properly then with the flow of the urine the pathogen will pass out of the body [11]. If a patient with UTI intakes the cranberry in the form of juice, then it is going to be helpful as it will inhibit the growth of both resistant and sensitive strains of the bacterium. It supplies an added benefit by resisting the attachment of the bacterium in the gastrointestinal mucosal [11].

Figure 5 [15]

Cranberry – The most efficient medicinal plant for UTI treatment

Among all these medicinal plants, cranberry is considered the most effective against the microbe causing Urinary Tract Infections. As it prevents the development of biofilm formed by both gram-negative and gram-positive pathogens. The plant has phenolic compounds known as proanthocyanidins which are stable. These compounds function as anti-griping agents against *Escherichia coli*. The extracts and juices of cranberry not only inhibit the growth of *E. coli* but also resists *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae,* and *Proteus mirabilis* which are pathogenic enough to cause UTI [11].

The compound proanthocyanidins have both A-type and B-type linkages. Comparing both the linkages it is seen that A-type linkage shows better anti-adhesive power than B-type linkage which prevents the attachment of fimbriae of the pathogenic bacteria on the wall of the bladder. This in turn prevents *E. coli* from infecting urinary mucosa [11].

Not only do proanthocyanidins act in the prophylactic effect in UTI, but other compounds are effective while treating the infection. The biologically active agents are anthocyanidin, catechin, flavonols, myricetin, quercetin, and phenolics [11].

The cranberry extracts of the different formulations launched in the market are available either in the form of juices or in tablets which are given in a measured dose. Cranberry indeed has a high medicinal effect, but it only works when it is combined with antibiotic treatment as it gives a prophylactic effect [11].

Development of vaccines to treat Urinary Tract Infections

Vaccine development shows a new path in treating this notorious infection. The vaccines are made on the basis that they will teach the bladder to fight against the pathogen. The vaccine might be administered in the bladder directly. The antigen present in the vaccine is combined with an adjuvant which can remove the bacterial cells [10].

This technique is developed because the immune response was not enough to treat bladder infections. After all, the immune system only repaired the cells which were damaged, but it did not release any barrier cells which will be going to fight against the pathogen from surviving and reattack the bladder more than one time [10].

Conclusion

Urinary Tract Infections are irritating and notorious and occur once in the lifetime of people. The disease is curable but if it is not treated in the pilot stages then it can be fatal. The infection is restricted to the bladder only, the infection can spread to the kidneys, and pyelonephritis is the condition. From the kidneys, there are chances that infection can spread in the blood and cause sepsis. Different microorganisms can cause UTIs. The majority of them are *Escherichia coli*. The urine samples were evaluated to detect the microbe and it was found that all the biochemical tests were showing positive for *E. coli*.

The test also showed that the chances of contracting a UTI are more in women than men. The culprit is the anatomical structure of women where the length of the urethra is short which makes the path easy for the microbe to travel to the bladder. Also, there are some other reasons which make women more susceptible. Pregnancy is the reason why hormonal change causes a change in microflora and pressure on the bladder causing a problem in urinating due to this the bladder has some residual urine. The other reason is menopause where the estrogen level drops which makes the are dry. The infection can reoccur because the microbe first attaches itself to the epithelial cells of the bladder then it disintegrates the epithelial surface and lives inside it.

The disease can be treated by using antibiotics but nowadays these antibiotics are becoming resistant because the pathogenic microbe has developed a mechanism where it can resist the effect of antibiotics. The sample showed that out of twenty-three only nine antibiotics were sensitive i.e., 60% were resistant. Various alternative ways are coming for the treatment of UTIs where the use of medicinal plants is at the highest rank. The plant which showed the maximum effect is *Vaccinium macrocarpon* also known as cranberry. These alternatives should be taken alongside antibiotic treatment. Vaccines are on the way to solving the problem, as they are prepared in a way that not only teaches the bladder to replenish the lost cells but also to produce a barrier against the pathogen.

The latest technology in health care is the use of artificial intelligence where all the data is being put and set up by an algorithm that will very efficiently diagnose the disease. For the diagnosis of Urinary Tract Infection. The most efficient artificial intelligence is ANN among many others to diagnose the infection with the early symptoms.

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