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Biotechnology of the Diagnosis Urinary Tract Infections: Review

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ABSTRACT

Urinary tract infection is one of the most common diseases in the world caused by bacteria, as it affects both gender and all ages, ranging from acute to chronic. For this reason, the need to evaluate methods for diagnosing infections is very necessary. In this review eight different diagnostic techniques for diagnosing urinary tract infections were discussed, evaluated and compared, and their advantages and disadvantages were identified. And it turned out in general we can rely on diagnosis using nanotechnology, Biosensing, and Endoscope technology Regardless of their disadvantages, they are more efficient and accurate in diagnosis than other technologies.

Keywords: Urinary Tract infection, Microbiology, Diagnosing, Infection

1 Introduction

The urinary system is one of the most vital organs of the human body, one of its responsibilities is to control the balance of fluid levels in the blood, thus controlling blood pressure and its pH, and maintaining the amounts of salts in the bloodstream [1]. Urinary tract infections can be considered one of the common diseases, even the most common in the world, for both sexes and all ages even children [2], the reason for this is that the urinary tract not only allows urine to exit, but also germs can enter through it in the opposite direction, female are more susceptible to urinary tract infections, accounting for approximately 81% of reported infections [3] The reason for this is due to the nature of the anatomical structure of women, where the distance between the excretory opening and the urinary opening is close [4]. In most cases, Escherichia coli bacteria are the cause of infection, with a rate between 80 – 90% [5]. At the present time, treating urinary tract infections is somewhat difficult, this is due to the development of antibiotic-resistant bacterial strains, Therefore, the patient must be given increased doses of antibiotics of different types and on a wider spectrum, which leads to more resistance [6]. Until now, the GUE method and Urine culture remains the prevailing methods in laboratories for diagnosing UTI [7], But it does not give accurate and certain results. The reason for this is because the GUI cannot explain the cause and location of the infection in the urinary system. Moreover, a large percentage of the results of this test are due and depend on the laboratory lark in conducting the analysis and his experience also in microscopic diagnosis [8]. As for the test Culture may give negative results if the patient was taking antibiotics before the examination [9]. World Health Organization (WHO) studies have shown that the infection rate increases among girls at school age [10]. As for uncircumcised boys, they are 10-12 times more likely to suffer from urinary tract infections compared to circumcised boys [11]. The reason is that uncircumcised boys are more susceptible to urinary tract infections because foreskin it is a home for microbes to accumulate [12].

2 Methods of diagnostic

2.1 Clinical diagnosis

It is one of the types of examinations that the specialist performs in direct physical contact with the patient, looking for any visible signs on the patient that would give him an indication of a urinary tract infection [13]. In this type of test, many signs appear on patients that may be useful to the specialist doctor in diagnosing urinary tract infections, or there may be symptoms or clinical signs similar to diseases other than urinary tract infections (Table 1)

. In this case, the specialist doctor must be very accurate with the diagnosis and not rely solely on just one sign [14].

Table 1. Symptoms and symptoms similar to urinary tract infections.

Symptoms (Signs)	Similar Symptoms
Dysuria	Prostatitis [15]
Bladder Pain	Interstitial cystitis [16], Bladder Wall Stiffness [17], Bladder Cancer [18]
Loin pain	Polycystic ovary syndrome [19,20] Appendicitis [21]
Bloody Urine	Prostatic hypertrophy [15,22]
Discharge from the Urinary Opening	Testicular Inflammatory [23]
Fever	Infections in general [24]
Nausea	Iron, ferritin, Hemoglobin deficiency or H.pylori Infection [25]
Dark Color Of Urine	Hepatitis [26]
Density Of Urine	Diabetes Insipidus [27], Dehydration [28]
Appearance Of Urine	Increase protein levels [29], Eclampsia [30]
Smell Of Urine	Dehydration [28]
Frequent Urination	Diabetes mellitus [31]

2.2 *General urine examination*

It is one of the most common types of examinations for urinary tract performed in medical laboratories [32]. Through it, we know whether the patient is suffering from urinary tract infections, in addition to knowing the chemicals materials in the urine, in addition to detecting the presence of solid materials such as crystals [33]. The GUE is divided into three main parts: physical examination which depends on sight and through which it can be known and recorded Color, Odor and Aspect [34]. Chemical examination this is done through a strip containing squares for the reactant on which the result appears after dipping it in urine, it is compared with reference Range, which includes Sp. Gravity, Reaction (PH), Protein, Glucose, Ketones, Nitrite, Bilirubin, Urobilinogen, Leucocytes and Blood (Fig.1). These tests can give an indication of other systemic disorders such as kidney and liver functions [35].

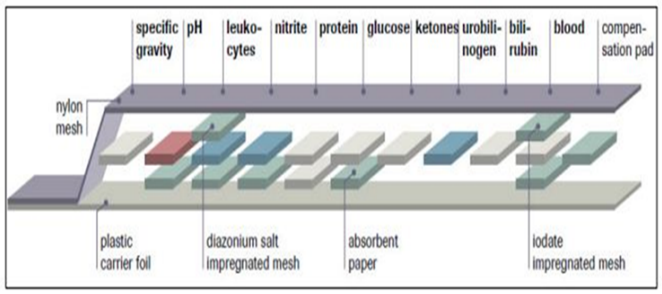

Fig. 1. A cross-section of a urine strip showing the test areas. (Source: Roche Diagnostics USA).

Microscopic examination this part depends on the microscopic diagnosis and the examiner's skill and experience in determining what appears on the slide after treating the sample in a centrifuge and examining the sediment includes Pus Cells, RBCs, Epithelial Cells, Mucus, Bacteria, Crystals, Casts and Others (Table 2, Fig.2) [36,37].

Table 2. GUE parts and reference range.

Physical Examination	Reference Range
Color	Yellow
Odor	Aromatic
Aspect	Clear
Sp. Gravity	1000
Chemical Examination	
Reaction	Acidic
Protein	Absent
Glucose	Absent
Ketones	Absent
Nitrite	Absent
Bilirubin	Absent
Urobilinogen	Absent
Leucocytes	Absent
Blood	Absent
Microscopic Examination	
Pus Cells	0 - 1 / HPF
RBCs	1 - 2 / HPF
Epithelial Cells	Absent
Mucus	Absent
Bacteria	Absent
Crystals	Absent
Casts	Absent
Others	Absent

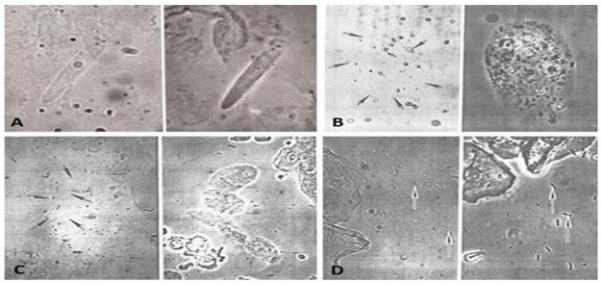

Fig. 2. Some models seen under a microscope A. Hyaline casts, B. A cast containing fatty droplets, C. Renal tubular epithelial cells, D. Squamous epithelial cells and bacteria [38].

2.3 *Urine culture*

Urine culture is one of the most important and common methods for diagnosing microbes in the urinary tract and testing their sensitivity to various antibiotics [39]. However, all urine samples were cultured without any clinical signs supporting the presence of urinary tract infections it can lead to unnecessary testing that increases cost and burden on the patient [40], therefore, it is necessary to confirm clinically whether a urinary tract infection is present before performing a urine culture. The urine is cultured on culture media, and then the bacteria that grow on the differential media are diagnosed, bacterial diagnosis is carried out by microscopy in addition to biochemical tests [41]. The sensitivity of isolated bacteria to various antibiotics is usually measured by the Kirby-Bauer method (disc diffusion method), which is the most widely used method, while Miller-Hinton medium has been used as a nutrient-rich medium for bacterial growth [41,42]. One of the advantages of this type of testing is prescribing the appropriate antibiotic for the bacteria that has been diagnosed and avoiding prescribing inappropriate antibiotics for the patient. This in turn reduces the cost and keeps the patient's life away from the risk of wrong treatments [43].

2.4 *Ultrasound*

It is one of the types of diagnosis of urinary tract infections for all ages and genders, as it can be used in newborns and adults alike [44]. This technique has many advantages, including non-surgical intervention, easy to use, can be applied to newborn patients and it is easy to replicate [45]. It is possible to diagnose infections in the lower part of the urinary tract, such as cystitis, urethritis, or ureteritis. It is also possible to diagnose infections in the upper part of the urinary tract, such as kidney pelvis infections or nephronitis, using this technique [46]. It is also possible to use this technology to monitor the severity of infections before and after the patient takes treatments, that is, to follow the condition and development of inflammation [47].

2.5 *Endoscope*

It is one of the techniques used in diagnosing and treating urinary tract infections [48]. It is a tube that contains a small high-resolution camera at the end, which is inserted carefully and slowly through the urinary opening after placing a local anesthetic in the area. It can be used in hospitals in operating rooms during general anesthesia [49]. An endoscope is inserted through the urinary opening to detect infections, cancers, stones, or eradication tumors in any parts of the lower and upper urinary system [50]. Artificial intelligence has begun to enter the medical field, specifically in endoscopy, to assist the doctor in treatment, diagnosis, and performing tasks in surgical operations [51]. There are two main types of endoscope: the rigid endoscope [52], which is usually used to examine the bladder, and the flexible endoscope, which is used for the ureters and kidneys [53].

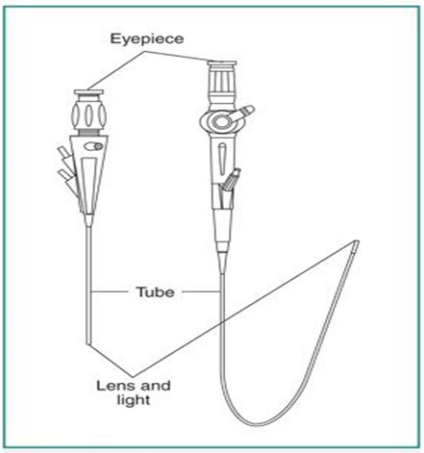

Fig. 3. Rigid endoscope and flexible endoscope. (Source: National Institute of Diabetes and Digestive and Kidney Diseases).

2.6 *Biosensing*

Due to the developments in the field of medicine, there has been a need for modern diagnostic techniques that provide less effort and less cost for patients and workers in hospitals and medical laboratories, therefore, devices for analyzing samples electrochemically were developed [54]. The biosensor works in a simple way to analyze urine samples to search, detect and analyze any information about their composition and components by converting biological responses into electrical signals [55]. Biosensors are one of the types of new and innovative biotechnology that are mainly used to detect cellular substrates [56], which include proteins, enzymes, hemoglobin (Hb), various chemicals such as toxins, and various pathogens [57]. Commercial biosensing devices were first sold on the market in 1970, and seven years later, the Food and Drug Administration (FDA) gave the green light to apply this test to test the final product on clinical samples to detect

pathogens [58].

2.7 *Nanotechnology*

Nanotechnology is considered one of the modern techniques in diagnosing and treating many diseases, including urinary tract infections, its works at the nanoscale level of materials [59]. Due to the modernity and development of this technique and its ability to diagnose many substances such as proteins and nucleic acids, in addition to its low cost and very low error rate, this technique is one of the best techniques used in diagnosing and treating urinary tract infections [60]. The principle of action of nanoparticles depends on their small size and very high sensitivity, as these particles are coated with artificial antibodies so that they only adhere to biological particles, DNA, proteins, or other biological particles in the human body, and they cannot adhere to other biological particles, and when these bind Proteins or other nanobodies coated in their conductivity will change, and thus this nanobiosensor can be used to detect a large number of diseases in their early stages. One of these materials used in the process of diagnosing urinary tract infections is copper NPs, and the reason for its use is due to its oxidation and reduction property, where particle diameters from 7 to 12 nanometers are usually using, where several types of bacteria can be diagnosed, such as: Escherichia coli, Klebsiella pnemoniae, Pseudomonas aeruginosa, Proteus vulgaris, Staphylococcus aureus, Proteus mirabilis [61]. Other substances that have the ability to diagnose urinary tract infections are silver [62], zinc oxide [63], and selenium [64].

2.8 *Artificial intelligence (AI)*

It is considered one of the types of advanced and modern scientific technology that has been widely used in many fields, including medicine, especially in the field of early diagnosis [65]. Artificial intelligence has the potential to provide results in the medical system in terms of diagnosing diseases [66]. In turn, artificial intelligence provides good tools that can be applied in the field of medical care to detect data accurately, and this data can then be translated and interpreted by specialized doctors to identify and diagnose clinical problems [67]. Many recent studies and reviews have primarily reported on the performance of AI at the diagnostic level, such as identifying and diagnosing diseases [68]. However, many of these studies are about developing and updating artificial intelligence programs and tools and their performance, but there is a noticeable lack of studies that address the role and impact of artificial intelligence used at the clinical level on patient safety.

3 Discussion

After presenting the most common methods of diagnosing urinary tract infections in hospitals and medical laboratories, now we can evaluate them and show the advantages and disadvantages of each method and give a point for each advantage. Therefore, we can compare and differentiate between them on the basis of completion time, patient comfort, cost, availability, accuracy in diagnosis, efficiency, Requires skills (Table 3).

If we want to compare the methods of diagnosing urinary tract infections in terms of time, we find that clinical diagnosis, GUE, and ultrasound diagnosis are among the fastest diagnostic methods because they do not require a complex techniques [69]. As for the comfort of the patient, we find that the patient is more comfortable when using clinical diagnosis because he only needs the patient to sit in front of the specialist doctor and the method of urine culture because it only requires bringing a urine sample to the laboratory and diagnosis using artificial intelligence and the nanotechnology method and diagnosis using ultrasound waves. Regarding cost, clinical diagnosis, GUE, and ultrasound are the least expensive techniques because they do not require the use of equipment. Regarding availability, clinical diagnosis, GUE, urine culture, and diagnosis using ultrasound are the most available techniques in hospitals and private clinics because they do not require special requirements in third world countries and developing countries [70]. As for the accuracy of the diagnosis, the clinical diagnosis cannot be completely relied upon due to the presence of symptoms similar to those of urinary tract infections as in (Table 1). As for the GUE, it cannot be completely reliable 100% because the genital tract is shared with the urinary tract in males. It is possible that infections may appear in the urine stream and under the microscope, but they are due to infections in the genital tract and not in the urinary tract. Also, we cannot rely on urine culture technology completely in diagnosis unless we provide it with an ideal environment, such as lack of pollution, taking the sample in a correct way, and a correct method of diagnosis in biochemical tests [71]. As for efficiency, all the techniques used in diagnosing urinary tract infections can be efficient, but the most efficient techniques of all are Nanotechnology, Biosensing, and Endoscope, because the error rate in them is very small. Regarding skill requirements, all of the techniques mentioned in this review require skilled people to complete or accomplish them, except for the diagnosis method and the artificial intelligence method, which leaves it to the artificial intelligence to do so [72].

Table 3. Compare the evaluation techniques used in the review.

	Time	Patient Comfort	Cost	Availability	Diagnostic accuracy	Efficiency	Requires skills	Total
Clinical Diagnosis	1	1	1	1	0.5	0.5	1	6
GUE	1	0.5	1	1	0.5	0.5	1	5.5
Urine Culture	0	1	0	1	0.5	0.5	1	4
AI	1	1	0	0	0.5	0.5	0	3
Nanotechnology	0	1	0	0	1	1	1	4
Biosensing	0	0	0	0	1	1	1	3
Endoscope	0	0	0	0	1	1	1	3
Ultrasound	1	1	1	1	0.5	0.5	1	6

4 Conclusion

This review can be a reference for doctors and laboratory workers to facilitate the process of comparing methods for diagnosing urinary tract infections. Due to the large number of cases of urinary tract infections in the world for both sexes and all ages, there is an urgent need for methods of diagnosing these infections and evaluate these methods, compare its, and know the advantages and disadvantages of all of these methods. In this review, I conclude that each type of technology used in diagnosing urinary tract infections has its advantages and disadvantages, but in general we can rely on diagnosis using nanotechnology, Biosensing, and Endoscope technology. Regardless of their disadvantages, they are more efficient and accurate in diagnosis than other technologies. It is recommended to use more than one method for diagnosis to reduce the error rate. It is also recommended to search for other new techniques that can combine the advantages of all the mentioned techniques, as they are low in cost and comfortable for the patient, the time for completion is short, and they are available in all health care settings and in all developing countries, third world countries, and developed countries alike, and their efficiency is high and the accuracy of their diagnosis is high.

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Ethical consideration: The study was approved by Al-Muthanna University, Al-Muthanna, Iraq.

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