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Study of Biochemical Markers Related to Urinary Tract Infection UTI

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Annotation: Urinary tract infection is an infection that begins with the urinary system. The UTI is one of the common diseases, as it increases in females. More than males, at a rate of 56% in females and 44% in males, due to the shorter urethra in females than in males. This study was designed to investigate some biochemical parameters related to UTI, where this disease is one of the most serious health problems that face large numbers of people annually. The research was included the collecting results of the following tests (calcium oxalate, uric acid, urea, creatinine, and C-reactive protein).

In addition, the data for 100 participants, who were included 51 women (28 patients and 23 healthy control) and 49 men (29 patients and 20 healthy control), were collected from the Hospital of Imam Hassan (AS) at the holly city of Karbala during the period from November 14, 2021, to January 13, 2022 (three months), of both sexes and in different age groups. The results were also statistically analyzed using Chi-square, T test and Man-Whitney tests. The results showed the following:Females are more susceptible to infection compared to males. In the uric acid test, no change was observed in the

results, whether for patients or normal persons. In the test of urea and creatinine, an increase in their concentrations was observed by a relatively large percentage for patients.In the calcium oxalate test, the statistical analysis of the data shows that there is a significant difference between healthy and sick patients. In the CRP test, an increase in its concentration in patients.Consequently, it can be concluded that the chances of women getting a urinary tract infection are more than men, because the nature of the urinary system of women is different from that of men.

Keywords: Urinary tract infection, biochemical markers, calcium oxalate, creatinine, C-reactive protein, gender susceptibility.

1.1. Introduction:

The urinary system in the kidneys includes the bladder, ureters, and penis duct. This system is one of the important organs in the human body due to the nature of its functions. The unitary system plays main roles in purifying the blood from harmful substances and excess substances that the body needs and disposing of them in the form of urine.

The examination of urine provides specifications and contents as good indicators that reflect the normal or abnormality of pathological and physiological infections. In addition, this examination of urine can indicate to the functions of the kidney in maintaining the natural balance of body [1].

The urinary tract infection (UTI) may occur by widespread using of antibiotics. Intake of these antibiotics for an extended period can lead to increase the resistance of microorganisms and the emergence of strains that have the high tolerance to antibiotics. [1]

Bacteria are the main cause UTI, among other organisms responsible for the diseases [2]. *E. coli* is one of the most important types of gram-negative bacteria which can isolate from urine samples of infected people [3]. Furthermore, *staphylococcus coli* has mechanisms of antibiotic resistance [1].

Any defect in the urinary system that leads to barrier the stream of urine, and hence increases the susceptibility to UTI due to the stagnation of urine by providing the opportunity of growing up the bacteria. This disease is one of the common diseases during childhood [4]. In addition, the use of catheter tubes, which reach the bladder through the urethra, is one of the reasons of this disease, by increase the growth of bacteria into the bladder [5].

Women, who have contracted the disease are more susceptible to repeat the infection. Many studies indicated to the risk of recurrence of infection in women due to the presence of bacteria auxiliary factors in the cells lining the wall of the urinary system that help in the adhesion of bacteria and then their transfer to the urinary system. Other studies indicated that there are special patterns of blood groups that may have a role in the disease. The prevalence of the disease varies according to geographical conditions and health conditions [6], where poor health conditions and malnutrition affect the occurrence of other infections [7].

Urinary tract infection is a common disease that people suffer from, and this the disease may be secondary to the presence of other diseases, where the infection may be alone or be accompanied by other diseases such as cases of gastritis, cases of malnutrition and cases of acute respiratory infection [8]

Urinary tract infection is related to patients' conditions, genders, and ages more than to the pathological symptoms of different UTI cases [9].

Therefore, UTI is the most serious health problems confronting millions of people, especially the women. Although this disease is not common among men, it is considered extremely dangerous if men are infected [10].

Inflammation often occurs by bacterial, viral, or fungal infection. Urinary tract infection occurs when the digestive gas bacteria in the anus and very close to the urinary tract outlet opening, which begins to grow and multiply, may cause inflammation as a result of one type of bacteria such as *E.coli*. Inflammation can move from the penis duct to the bladder and then to the kidneys when untreated the inflammation. Consequently, it may be transmitted in other ways, as the bacteria can move from the blood to the kidneys [11].

1.2. Kidney installation:

The kidneys are a reddish-brown, which like the bean shape, and weighing about 150 grams in adults. The kidneys are located on both sides of the spine in the upper lumbar region and are partially protected by false ribs (XI and XII). The kidneys are located outside the peritoneal cavity, where they are located between the parietal peritoneum and the outer body wall (that is, outside the parietal peritoneum, as well as the ureter attached to it, and the adrenal glands). The outward-facing side of the kidney is convex, while the side directed toward the midline of the body has a concave indentation, called the hilus, which leads into a space called the sinus. This space is occupied by the ureter, artery, and renal vein before each of the latter veins significantly bifurcates, as shown in Fig. 1.1.

The kidney is surrounded by three layers of supportive tissue: the inner part, called the renal capsule, is transparent and prevents infection from spreading to the kidney from adjacent tissues, and the middle one, called the adipose capsule, suspends the kidney in place against the muscles of the trunk and acts as a protective cushion for the blows. As for the outer, the fascia of the kidney is called the renal fascia. It is fibrous and dense and surrounds the adrenal glands and attaches all these organs to the surrounding structures.

The anterior section of the kidney, as shown in Fig. 1.2, it can be observed the presence of three distinct regions in the kidney, starting from the outside and towards the inside, which are the cortex of bright red color and granular in appearance, followed by the medulla of red-brown color with a striped appearance on the inside. Cone-shaped structures called renal pyramids. The base of each pyramid is directed towards the cortex, while its apex, the nipple of the kidney, is directed towards the pelvis. The longitudinal planning of the pyramids and the medulla is explained by the fact that the pyramids are formed from blocks of urine collecting channels that run almost parallel. The pyramids are separated from each other at the base by renal columns consisting of an extension of the cortex inward to form a kind of hat that surrounds the pyramid. One pyramid and the surrounding cortical tissue together form the lobe of the kidney, and the number of these lobes is about eight in each kidney. Finally, the cortex and medulla for each kidney consist of more than a million nephron units, and these together constitute the units that make up urine and will separate their structure and functions later.

As for the cups third region that makes up the kidney, called the pelvis, it is funnel-shaped and connects with the ureter that comes out with the navel of the kidney, and on its side closest to the medulla, the pelvis branches to form 2-3 large major calyces, each of which is divided into a number of small minor calyces. The sum of the small cups in each kidney are 8 – 18.

Small cups embrace the nipples of the pyramids, so the urine that reaches the urine collecting ducts is emptied at the nipples directly into the small cups and then moves to the large cups follow to the pelvis, and to the ureter. The small and large calyxes, pelvis, and ureters contain smooth muscles that contract regularly to push urine toward the urinary bladder in a peristaltic-like motion.

Every minute, about a quarter of the cardiac output from the blood reaches the kidneys (1200 milliliters/minute). The renal artery supplies blood directly to the kidney from the aorta. Prior entering to the kidney, the renal artery branches into five segmental arteries, Fig. 1.3. Each segmental artery, when entering the kidney sinus, is divided into several lobar arteries, which in turn is divided into several interlobar arteries passing between the pyramids heading towards the cortex.

Each of the latter branches have several afferent arterioles, which supply the blood to one of the renal units (nephrons) and exits from it in the form of an afferent arteriole. Therefore, expect that the number of incoming or outgoing arterioles will reach more than one million arterioles.

The veins in kidney have the same course and name for the arteries. The interlobular veins (cortical radial veins) form the arch veins, and these form the interlobular veins that come together to form a direct renal vein, as there are no lobar or segmental, the renal vein drains into the inferior vena cava. The nerves connecting to the kidneys and ureters come from the renal plexus, which includes knots and nerve fibers that follow mostly the sympathetic system, as they exit from the lumbar and thoracic visceral nerves and then pass parallel to the renal artery to reach the kidney. The main function of these nerves is controlling the blood flow to the renal units, which consequently affects the work of the kidneys in the formation of urine, and this effect is usually done by controlling the diameter of the blood vessels in the kidney [12].

1.3. Renal Function Tests:

The blood urea level is an inaccurate indicator of the state of renal function due to it is affected by the level of proteins which formed by the metabolic capacity of the liver, and the rate of renal perfusion Fig.1.4. The level of serum creatinine is also a reliable indicator for the renal function. Creatinine is produced by the muscles at a constant rate and is almost completely filtered through the renal glomeruli. Since an exceedingly small part of creatinine is secreted by tubular cells, creatinine clearance gives an acceptable approximate value for the glomerular filtration rate. If the muscle mass remains constant, the change in creatinine concentration indicates to presence a change in the glomerular filtration rate. However, in typical cases, an increase outside the normal range does not occur until after the glomerular filtration rate drops by about 50%. In addition, the measurements of serum creatinine concentration may provide the false impressions about renal function in patients who have unusually small muscle mass (and sometimes in those who have exceptionally large muscle mass). Currently, a more accurate measurement of EFR can be easily done by measuring the clearance of Cr-tagged EDTA. This test has replaced in clinical practice the measurement of inulin clearance. Tubular function tests, including the ability to condense urine, the ability to excrete water-carrying capacity, and the ability to excrete acid, are useful and valuable in some circumstances [13].

1.4. Kidneys Role in Balancing Body's Components:

1.4.1. The role of kidneys in balancing sugar in blood

The kidney's involvement in glucose homeostasis was first described in 1930s [14]. Despite the large body of evidence amassed over the ensuing years, the kidney is still often overlooked as an important player in glucose metabolism. However, glucose homeostasis is likely to increase in the near future because novel glucose-lowering- drugs are being developed that target one aspect of renal glucose handling, namely reabsorption of glucose from the glomerular [the sodium–glucose co-transporter (SGLT2) inhibitors]. From 1989 to present, Medline use the terms 'Renal gluconeogenesis', renal glucose. The human kidney is involved in the regulation of glucose.

Homeostasis and in abnormalities found in diabetes mellitus via three different mechanisms:

(i) Release of glucose into the circulation via gluconeogenesis.

(ii) Uptake of glucose from the Circulation to satisfy its energy needs.

(iii) Reabsorption into the circulation of glucose from glomerular I literate to conserve glucose carbon.

Few people paid attention to the role of the kidneys in glucose homeostasis. However, similar to the liver, kidney plays a vital role in ensuring that energy needs are met during fasting. Approximately 180 liters of plasma are filtered by the kidneys every day. In addition, the kidneys play a key role in absorbing all filtered glucose. The glomerular filtration rate is 180 liters per day, the plasma glucose concentration is 5 millimoles/liter, and the kidneys filter approximately 162 grams (900 millimoles) of glucose per day, which helps maintain normal fasting blood glucose (FPG) levels (~5.6 mmol/l) [17,18]. The kidneys have developed a very effective adaptive system, including sodium-glucose cotransporter (SGLT)2 and SGLT1, to recover all filtered glucose. Diabetes occurs when the plasma glucose level exceeds the maximum reabsorption capacity of the renal SGLT1. transport system. Glycosuria occurs at expression and activity of SGLT2 the transport protein responsible for 80–90% of renal glucose reabsorption are increased in type 2 diabetes [19-21]. Therefore, the kidneys reabsorb higher-than-normal amounts of glucose into the blood, causing and maintaining hyperglycemia. Long-term elevated plasma glucose levels can exacerbate insulin resistance and β-cell dysfunction (*i.e.*, glucotoxicity), further contributing to the abnormal glucose homeostasis that characterizes type 2 diabetes [15,16,18].

1.4.2. The Role of Kidneys in Balancing Salts in Blood

Sodium chloride is commonly called dietary salt, which is essential to human body. However, intake high amount of salts can raise blood pressure, which can damage the body in unusual ways over time. High blood pressure has been associated with the heart diseases, stroke, kidney failure, and other health problems.

Researchers have long believed that the level of salt in human can be controlled by straightforward: when the salt levels are too high, the brain is stimulated to make thirsty. To resolve this issue drink more and excrete more urine, through which the body expels excess salt.

To gain insight into this process, Jens Titze and his team at the University of Erlangen-Nuremberg in Germany took the opportunity to study men participating in a simulated space flight program. Between 2009 and 2011, they tightly controlled the daily salt intake of 10 men simulating a flight to Mars: four in a 105-day pre-flight phase and six others for 205 days. The men were given 12 grams of salt per day, 9 g/day, or 6 g/day for 30–60 days. The researchers collected all the men's urine for testing.

The scientists were surprised to find that, whatever the level of salt consumed, sodium was stored and released from the men's bodies in roughly weekly and monthly patterns. The team uncovered similar rhythms for the hormone's aldosterone, which regulates sodium excretion from the kidney, and glucocorticoids, which help regulate metabolism.

Titze, now at Vanderbilt University Medical Center, continued to examine the long-term control of sodium and water balance in the men. To better understand the mechanisms at work, his team also performed experiments in mice. Their latest results appeared in two papers on May 1, 2017, in the Journal of Clinical Investigation. The work was funded in part by NIH's National Heart, Lung, and Blood Institute (NHLBI) and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Changing salt intake affected levels of both aldosterone and glucocorticoids, the hormones found to rhythmically control the body's salt and water balance. These, in turn, had a number of

interesting effects in the body. Increasing salt intake increased sodium excretion, but also unexpectedly caused the kidney to conserve water. Excess sodium was thus released in concentrated urine. This method of protecting the body's water was so efficient that the men actually drank less when their salt intake was highest.

These results show that the body regulates its salt and water balance not only by releasing excess sodium in urine, but by actively retaining or releasing water in urine. The advantage of this mechanism is that the long-term maintenance of body fluids isn't as dependent on external water sources as once believed.

The researchers found that the kidney conserves or releases water by balancing levels of sodium, potassium, and the waste product urea. This may be what ties glucocorticoid levels to salt intake. A high salt diet increased glucocorticoid levels, causing muscle and liver to burn more energy to produce urea, which was then used in the kidney for water conservation. That also led the mice to eat more. These salt-driven changes in metabolism may thus partly explain why high salt diets have been linked to diabetes, heart disease, and other health problems that can result from the condition known as metabolic syndrome.

A high salt intake may predispose to metabolic syndrome, Titze says. More work will be needed to better understand these mechanisms [22].

The rate of the renal sodium excretion is a function of numerous regulators, *i.e.*, factors shown to cause graded responses in vivo. Regulators may be mediators and modulators. In the present context, a mediator is a regulator with signal intensity primarily dependent on the TBS causing graded, monotonous responses in renal sodium excretion. A modulator may also cause graded changes in sodium excretion, but the signal strength is not primarily coupled quantitatively to TBS. About the action of mediators on sodium excretion, principally different concepts exist. One is based on renal arterial pressure being the overriding mediator of sodium excretion, and that all other mediators operate via this "pressure natriuresis" mechanism Fig. 1.4. (Top). This means that increases or decreases in sodium excretion occurring at a constant renal arterial pressure-or even during antiparallel changes herein is an effect of pressure natriuresis assumed to be reset by the concomitant neurohormonal changes. This is also the case where the latter unquestionably affect renal tubular function. Anotherr concept includes parallel processing of the signals mediating renal sodium excretion Fig. 1.4. (bottom) allowing individual mediators to co-drive renal tubular handling of sodium and thereby to regulate sodium excretion by concerted actions. The latter concept Is open for analysis by way of mediators and modulators, and in these terms, renal arterial pressure is a modulator.

Concepts of regulation of renal sodium excretion. Top: dominance of the pressure natriuresis mechanism; increases in sodium excretion are driven by arterial pressure even when pressure is constant or decreasing because the pressure natriuresis mechanism is considered to be reset by concomitant neurohormonal changes. Bottom: parallel processing concept meaning that the signals mediating renal sodium excretion operate in parallel allowing individual mediators to co-drive renal tubular handling of sodium and thereby sodium excretion to become a result of concerted actions [23].

1.4.3. The Role of Kidneys in metabolism of Amino Acids

The kidneys play a position withinside the synthesis and interorgan change of amino acids. The quantitative significance of renal amino acid metabolism withinside the frame is not, however, clear. Evaluation right here the position of the kidney withinside the interorgan change of amino acids, with emphasis on quantitative aspects. The kidney takes up glutamine and metabolizes it to ammonia. This procedure is touchy to pH and serves to keep acid-base homeostasis and to excrete nitrogen. In this way, the metabolism of renal glutamine and ammonia is complementary to hepatic urea synthesis. Citrulline, derived from intestinal glutamine breakdown, is transformed to arginine through the kidney. Renal phenylalanine uptake is observed through stoichiometric

tyrosine release, and glycine uptake is observed through serine release. Certain administered oligopeptides (*e.g.,* glutamine dipeptides) are transformed through the kidneys to their constituent additives earlier than they may be utilized in metabolic processes. The kidneys play a critical position withinside the interorgan change of amino acids. Quantitatively, for numerous critical amino acids, the kidneys are as critical because the intestine in middleman metabolism. The kidneys can be crucial "mediators" of the useful results of specialized, disease-unique feeding solutions inclusive of the ones enriched in glutamine dipeptides [24].

The net renal metabolism of amino acids and ammonia in the post absorptive state was evaluated in subjects with normal renal function and in patients with chronic renal insufficiency by measuring renal uptake and release, and urinary excretion of free amino acids and ammonia. In normal subjects the kidney extracts glutamine, proline, citrulline, and phenylalanine and releases serine, arginine, taurine, threonine, tyrosine, ornithine, lysine, and perhaps alanine. The renal uptake of amino acids from arterial blood occurs by way of plasma only, whereas approximately a half of amino acid release takes place by way of blood cells. Glycine is taken up from arterial plasma, while similar amounts of this amino acid are released by way of blood cells. In the same subject's total renal ammonia production can be largely accounted for by glutamine extracted.

In patients with chronic renal insufficiency can note the following:

(a) The renal uptake of phenylalanine and the release of taurine and ornithine disappear.

(b) The uptake of glutamine and proline, and the release of serine and threonine are reduced by 80--90%.

(c) The uptake of citrulline and the release of alanine, arginine, tyrosine, and lysine are reduced by 60--70%.

(d) No exchange of glycine is detectable either by way of plasma or by way of blood cells.

(e) Exchange for other amino acid via blood cells disappear.

(f) Total renal ammonia production is reduced and not more than 35% of such production can be accounted for by glutamine extracted, so that alternative precursors must be used.

A 140% excess of nitrogen release found in the same patients suggests an intrarenal protein and peptide breakdown, which eventually provides free amino acids for ammonia production [25].

Renal ammonia metabolism and transport mediates the role in acid-base homeostasis. In contrast to most renal solutes, most of the renal ammonia excretion derives from intrarenal production, not from glomerular filtration. Renal ammonia genesis results from glutamine metabolism, which produces 2 NH_4^+ and 2 HCO_3^- for each glutamine metabolized. The proximal tubule is the primary site for ammoniagenesis, but there is evidence for ammoniagenesis by most renal epithelial cells. Ammonia produced in the kidney is either excreted into the urine or returned to the systemic circulation through the renal veins. Ammonia excreted in the urine promotes acid excretion; ammonia returned to the systemic circulation is metabolized in the liver in a HCO_3^{-2} consuming process, resulting in no net benefit to acid-base homeostasis. Highly regulated ammonia transport by renal epithelial cells determines the proportion of ammonia excreted in the urine versus returned to the systemic circulation. The traditional paradigm of ammonia transport involving passive NH_3 diffusion, protonation in the lumen and NH_4^+ trapping due to an inability to cross plasma membranes is being replaced by the recognition of limited plasma membrane NH_3 permeability in combination with the presence of specific NH_3-transporting and NH_4^+-transporting proteins in specific renal epithelial cells. Ammonia production and transport are regulated by a variety of factors, including extracellular pH and K^+, and by several hormones, such as mineralocorticoids, glucocorticoids, and angiotensin II. This coordinated process of regulated ammonia production and transport is critical for the effective maintenance of acid-base homeostasis [26-39].

1.5. Urinary Tract Infection in General:

The urinary system is one of the important organs in the body, and any defect in the function of this system can affect the rest of the organs because it participates with the rest of the body's organs In regulating the volume and components of cellular fluid, and works to remove toxic waste from the blood in addition to its role in regulating the blood, and the concentration of ions in it. And then its participation in the formation of red blood cells and the representation of vitamin D [39].

The entry of the ureters into the urinary bladder and the presence of a valve that prevents urine from returning to the kidney again, and this mechanism helps the kidneys not to suffer from lower urinary tract infection (lower urinary tract infection), in addition to the acidity of normal urine, which is one of the main characteristics that prevents the growth of bacteria. The rapid flowing urine during the urination process works to remove the germs. However, this channel is invaded in some cases by a group of normal flora that function as opportunistic organisms also in addition to the main pathogens [40].

Urinary tract infections are the health problems that affect a large proportion of the human community, estimated at millions annually. Studies indicate that the rate of male infection with these infections Is lower than the rate of female infection because of the length of the urethra in males, which reduces the chances of colonization of the bladder by germs [41].

Urinary tract infections can be classified into:

1. Classification of urinary tract infection in terms of pathogenesis.

A. Complex urinary tract infection:

Proteus bacterial infections of the urinary tract are often associated with complex urinary tract infection in addition to catheterized patients and is usually associated with structural abnormalities in the urinary tract, obstructions and congenital malformations [42].

B. Uncomplicated urinary tract infection:

Uncomplicated urinary tract infection constitutes a large proportion of infections, and it occurs when there are no abnormal anatomical, functional and neurological changes and imbalances in the urinary tract so that the kidneys perform their functions normally, as well as it is not compatible with disorders that lead to a malfunction in the body's defense mechanisms, including infections uncomplicated urinary tract in turn both bacteria asymptomatic urine, cystitis and nephritis [43].

2. Classification of urinary tract infection according to the location of the infection

A. Upper urinary tract infection:

Includes inflammation of the nephritis and pelvis resulting from bacterial invasion of the parenchymal layer of the kidney [44].

B. *Lower urinary tract infection*:

It guarantees both cystitis and urethritis (45).

3. Classification of urinary tract infection according to the severity of the infection

A. *Primary infections*:

This type of infection occurs as a result of bacteria invasion and settlement in the urinary tract for the first time, accompanied by symptoms such as fever with the presence of purulent cells and evidenced by the presence of white blood cells [46].

B. *Recurrent infections:*

The reason for the recurrence of urinary tract infection may be due to the lack of adequate

treatment or non-adherence to treatment, In addition to the resistance of the pathogen to antibiotics [47].

C. Persistent infections:

These infections are known as a condition of the persistence of pathogenic bacteria after treatment, and this means that the focus of infection in the urinary tract has not yet been treated, and that the pathogen often settles in sites protected from the arrival of antibiotics, and protected sites are often anatomical abnormalities, urinary stones and bodies strange as urinary catheters [48].

D. Other causes and risk factors:

The urinary system consists of the kidneys, urinary tubes, bladder, and urethra. Each of these compounds plays an important role in the excretion of waste from the body.

The causes of urinary tract infection are usually the entry of germs into the urinary system through the urethra and then begin to multiply in the bladder.

Although the urinary system is designed in a way that is supposed to prevent this entry of prokaryotes, this defense system sometimes fails to perform its task. And when such a failure occurs, the germs take over and begin to multiply, causing a strong and severe infection in the urinary tract.

Most urinary tract infections appear in women mainly and affect the urethra and bladder.

In most cases, the cause is *E.coli*, this type of bacteria is usually found in the digestive system and intestines. All women are exposed to urinary tract infection because of the anatomical structure of the woman's body, especially because of the proximity of the origin of the urethra to the anus.

Catheterization predisposes to UTI and about 2% of hospital-acquired UTI cases are caused by urinary catheterization [49].

The implantation of the catheter may lead to the carrying of germs directly to the bladder through the space in it or through contact along the outer surface of the mucous membranes between the catheter and the urethral wall [50].

There are a number of factors that increase the risk of urinary tract infection, the most important of which are [51]:

I. Diabetes cases.
II. Multiple sexual relations.
III. Pregnancy.
IV. Use of some skin irritants.
V. Taking birth control pills.
VI. Excessive use of antibiotics.
VII. Enlarged prostate gland.

1.6. Urinary Tract Infections in Iraq:

There are various studies has focused on UTI in Iraq. The prior study was conducted to detect the urinary tract infections (UTIS) from patients in consultant of urinary tracts in Al-Khadimiya Teaching Hospitals Baghdad. A total of (544) specimens with positive urinary tract infections were collected from (1512) patients in consultant of UT during 12 months through a period commencing from January 2010 to December 2010. The results of microscopic examinations showed that UTIS were more frequent in female than male patients. The number of male patients were (176) (32.35 %), while female patients were (368) (67.65%). The results revealed that the

highest percentage of UTIS (60.66%) was recorded in adult patients (26 - 45) years. Moreover, the results showed that sexual activity of women play an essential role in UTI with a percentage of (43.38%) compared to other factors. Concerning the relation between the seasons and infection, it was found that UTIs recorded different rates during the seasons and the highest percentage (34.56 %) was recorded in spring while the other seasons recorded lower infections [52].

2.1. Methodology:

2.1.1. Materials

Table 2.1. Materials and the suppliers.

2.1.2. Collecting Data

The data of 100 specimens have been collected from Imam Hasan (AS) hospital in the city of holly Karbala during the period of 14th Nov. 2021 to 13th Jan. 2022 (three months). These samples were included 51 women (28 patients and 23 healthy control) and 49 men (29 patients and 20 healthy control).

2.2. General Urine Examination (GUE):

The GUE includes two main tests:

2.2.1. Chemical Tests

These tests include the following:

1. Check the pH for urine (acidic).
2. Check the color of urine (white, yellow, brown, red, etc.)
3. Check the density of urine (S.G. = 1.0005).
4. Check the situation of urine (clear or turbid).
5. Albumin test (check the protein).
6. Benedict's test (check the sugar).

2.2.2. Microbiology tests

After centrifuging the urine sample, the microbiological test is performed by using the microscope.

- *Calcium Oxalate*

Calcium oxalate and uric acid crystals can be detected by microscopic analysis of a urine sample. Where calcium oxalate salts appear in the form of an envelope or an oval shape or take the shape of bone, Fig. 2.1.

Figure 2.1. Picture of oxalate structure in urine under microscope**.**

- *Uric Acid*

As for uric acid crystals, they appear in the form of a prism, in the form of plates, or in the form

of a rosette of yellow or brown color, Fig.2.2.

Figure 2.1. Picture of uric acid structure in urine under microscope**.**

2.3. Blood Tests

The diagnosis of UTI depending on various examinations in blood, which include:

2.3.1. Uric Acid Test

The blood samples were collected in the tube as serum or plasma. The serum must be isolated after clotting or plasma as quickly as possible or two hours after the withdrawal process. The (2 ml) of the serum should be transferred to a standard tube.

- **Procedure:**

Using two tubes, a standard tube consists of 25µl the standard 1000µl of the reagent solution. The second tube contains 1000µl of the reagent solution in addition to 25µl of the sample. Both tubes were mixed well and then incubate for 5 minutes at a temperature of 37°C before reading the absorbance using UV-Vis spectrometer at a constant absorption UV wavelength, 295 nm.

2.3.2. Blood Urea Test

The blood samples were collected in the tube as serum or plasma. The serum must be isolated after clotting or plasma as quickly as possible or two hours after the withdrawal process. The (2 ml) of the serum should be transferred to a standard tube.

- **Procedure:**

Using two tubes, a standard tube consists of 10µl the standard 1000µl of the reagent solution. The second tube contains 1000µl of the reagent solution in addition to 10µl of the sample. Both tubes were mixed well and then incubate for 3 minutes at a temperature of 37°C before reading the absorbance using UV-Vis spectrometer at a constant absorption UV wavelength, 550 nm.

2.3.3. Serum Creatinine Test

The blood samples were collected in the tube as serum. The serum must be isolated after clotting or plasma as quickly as possible or two hours after the withdrawal process. The (2 ml) of the serum should be transferred to a standard tube.

- **Procedure:**

Using two tubes, a standard tube consists of 100µl the standard 1000µl of the reagent solution. The second tube contains 1000µl of the reagent solution in addition to 100µl of the sample. Both tubes were mixed well and then incubate for 5 minutes at a temperature of 37°C before reading the absorbance using UV-Vis spectrometer at a constant absorption UV wavelength, 680 nm.

2.3.4. C-Reactive Protein Test

After the sample is withdrawn, its contents are emptied into a special tube for CRP analysis, and then it is transferred to the laboratory, so that specialists can analyze it.

➢ **Procedure:**

✓ The blood sample is isolated by means of a centrifuge, in order to obtain a blood serum, where the analysis is carried out on the blood serum and not the blood itself.

✓ Apply 25µl of reagent to 25µl of blood serum on a latex slide.

✓ The specialist mixes them by moving the slide in a circular manner for 2 minutes.

➢ **Read the results:**

✓ If grains appear on the slide, the result is positive.

✓ In the absence of these granules, the result will be negative.

In the case of a positive result, another analysis called Titer is done, and it is in different proportions, in order to determine the extent of inflammation, by:

✓ The serum is diluted by adding 50µl of serum in 50µl of saline solution.

✓ Adding 25µl of diluted serum to 25µl CRP reagent, and then stir in the same circular manner for 3 minutes.

✓ If granules appear, the result is positive, and the same steps are repeated several times until the negative result is reached, but in the event that no granules appear, the result is negative.

✓ Method for determining percentages of CRP analysis

✓ After noticing the observations and laboratory steps, the specialist determines the proportions.

➢ **Method for determining percentages of CRP analysis:**

After observing the observations and laboratory steps, the specialist determines the percentages by:

✓ When the result is negative the first time, the ratio is -Ve.

✓ In the case of a positive result, and then a negative result, the ratio is: 6mg/dl.

✓ If the result appears positive in the first two steps, then a negative result appears, the result will be: 12mg/dl.

✓ And it was repeated in the same way of calculation, in order to get the exact percentage.

2.4. Statistical Analysis:

The data for this study were analyzed and presented as mean ± standard deviation, then analyzed using the GraphPad Prism-8 provided by the University of California San Diego. Mean differences between subjects with UTI and subjects' healthy volunteers' groups with normal distributions were analyzed with Student's t-test for independent samples. Statistical significance has been considered as $P < 0.05$.

Chapter Three

3.1. Result and Discussion:

The results of the following tests (calcium oxalate, uric acid, urea, creatinine and C-reactive protein) were collected for more than 100 patients of all ages and both sexes at Imam Hassan (AS) Hospital in Karbala, to study the biochemical markers related to urinary tract infection and the search results were as follows:

3.2. Calcium Oxalate:

In the calcium oxalate test, the Chi-squared test of data shows that there are significant differences among the healthy, few, and one plus groups ($p<0.0001$; $X^2 = 48.0$), Fig.3.1. This

result is corresponding with the previous study [52] that observed in the increase in the level of oxalate percentage of the patients compared with other study reported that patients with urinary tract infection had significantly higher urinary oxalate secretion than patients without UTI.

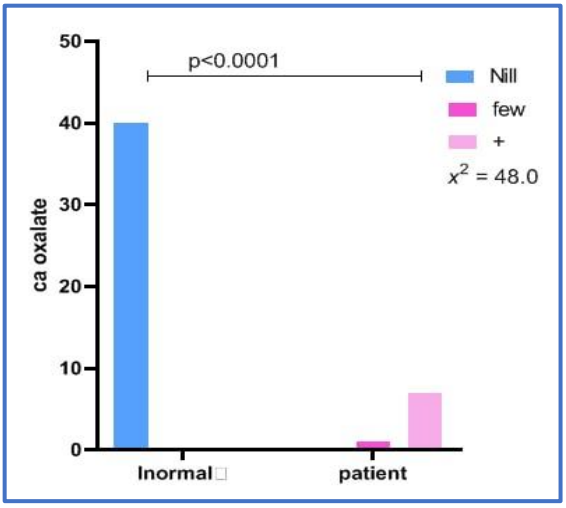

Figure 3.1. Chi-squared test of Ca-Oxalate.

3.3. Uric Acid:

The Chi-squared test for the collected data of uric acid test, also appears a significant differences among, healthy, few, and one plus groups ($p<0.0001$; X^2 =50.02), Fig. 3.2. These observed results are associated with previous study, which showed that 100% of patients had uric acid crystals in their urine sample [53].

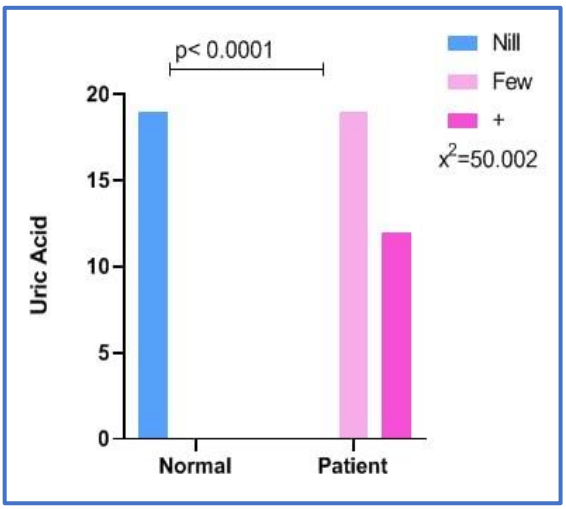

Figure 3.2. Chi-squared test of Uric Acid.

As for the comparison between the collected results of uric acid and Ca-Oxalate in both the men and the women in terms of the number of UTIs, the results of the research were in favor of women, Fig. 3.3, and this is consistent with another study where they concluded that Urinary infections are twice more likely to occur in females compared to males and its prevalence increases with increasing age [54].

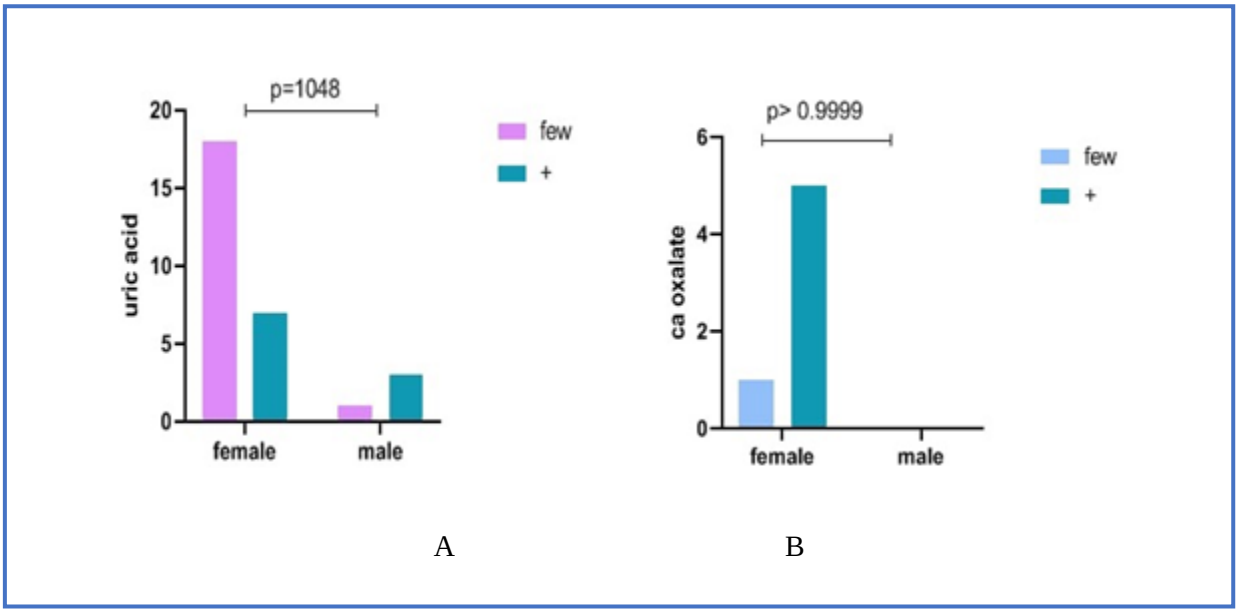

Figure 3.3. A- Fisher's exact test of Uric Acid. **B-**Fisher's exact test of Ca- Oxalate

3.4. Blood Urea and Creatinine:

The tests of urea and creatinine in patients appeared the clearly increase in the concentrations of them, which were observed by a relatively large percentage. These results are not corresponding with the prior study, which showed the levels of blood urea and creatinine were in the normal range for both the control and patients' samples [55]. The T-test for the collected data of blood urea and creatinine shows that there are significant differences between the patients and healthy groups ($p<0.0001$), Fig. 3.4.

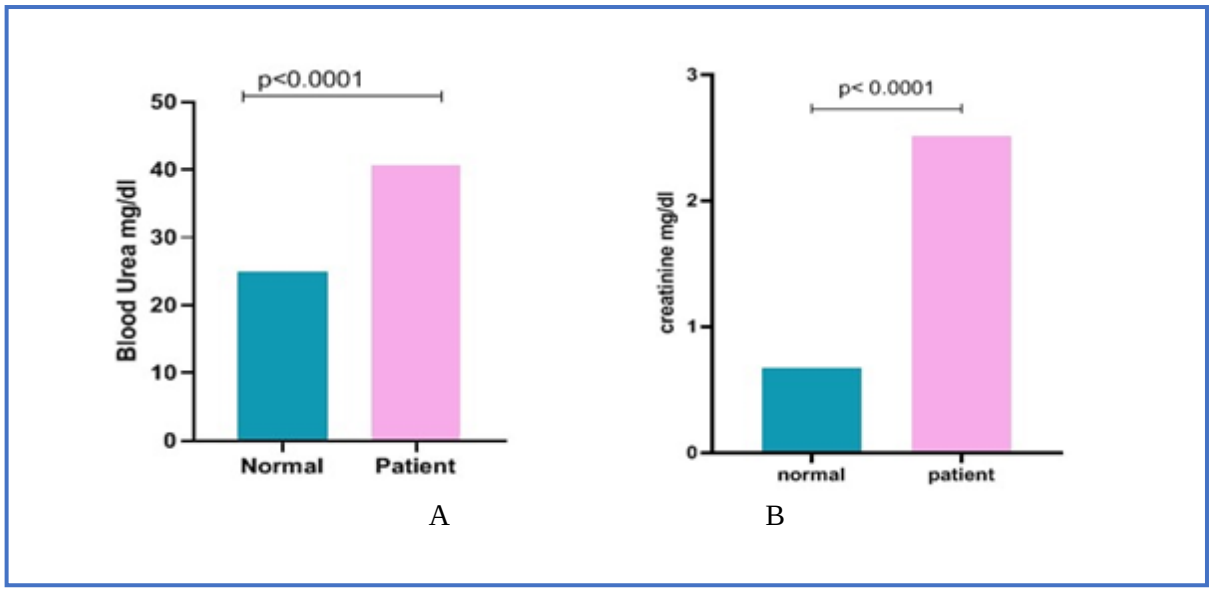

Figure 3.4. A- T-test for blood urea data.

B- T-test for serum creatinine data.

Elevation of urea and creatinine is not directly related to urinary tract infection except in chronic cases, but it is evidence of the safety of the kidneys, as both urea and creatinine rise in cases of dehydration, glomerulitis, kidney failure, kidney stones, prostate enlargement, bladder tumors, or due to consumption of large amounts of protein.

3.5. C-Reactive Protein:

In the CRP test, the result of T-test for the collected data appeared that a significant increase in the levels of CRP compered with the healthy controls, Fig. 3.5. This result is corresponding with

previous studies that applied in Europe and India. The studies reported a significant increase in C-reactive protein among UTI patients compared to those without UTI. An increase in CRP is commonly detected in UTIs due to Escherichia coli, Proteus, Klebsiella pneumoniae, Staphylococcus aureus and others [56].

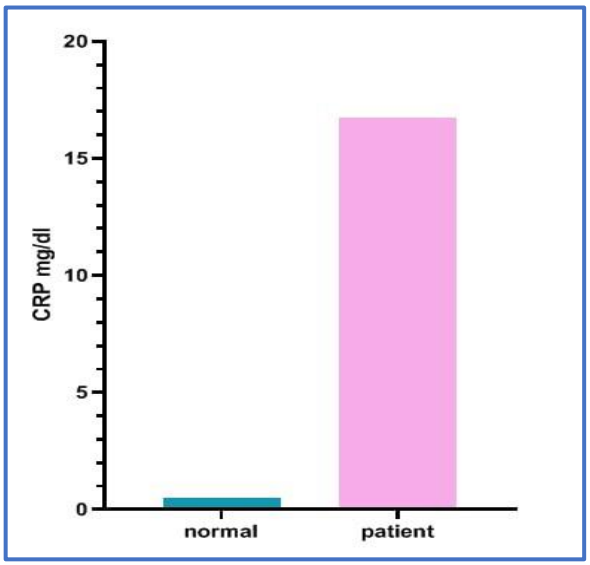

Figure 3.5. T-test for CRP data.

The chances of women getting a urinary tract infection are more than men, because the nature of the urinary system of women is different from that of men, as the urethra of women is shorter than that of men, and thus it is easier for bacteria to reach the bladder [57].

Conclusion

Based on the findings of this study on biochemical markers related to urinary tract infection (UTI), significant differences were observed in calcium oxalate, urea, creatinine, and C-reactive protein (CRP) levels between affected patients and healthy controls, while uric acid levels remained unchanged. The study confirmed that females are more susceptible to UTIs than males, likely due to anatomical differences. Elevated urea and creatinine levels indicate potential kidney function impairment, while increased CRP levels suggest an inflammatory response associated with UTIs. These findings highlight the importance of early biochemical marker assessment for UTI diagnosis and management. The study's implications suggest that biochemical markers can be used as diagnostic tools for detecting UTIs and monitoring kidney function, thereby improving patient outcomes. Further research is needed to explore the role of additional biochemical markers, the impact of antibiotic resistance on UTI prevalence, and the development of targeted therapeutic strategies to reduce recurrence rates, particularly in high-risk populations.

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