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Bacteriological Profile of Urinary Tract Infections and Antibiotic Resistance Profile in the Telagh Region (West Algeria)

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ABSTRACT

Urinary tract infection (UTIs) remains a very common pathology all over the world. It is the leading cause of nosocomial infection. It is with this in mind that we undertook a prospective descriptive and analytical study whose objective was to isolate and identify uropathogenic bacteria involved in urinary tract infection and monitor the profile of antibiotic sensitivity in urinary tract infection in the private laboratory of the Telagh region. In this context, the macroscopic examination, Strips and the Cytobacteriological examination of the Urines (ECBU) are among the most frequent microbiological analyzes carried out. the samples are analyzed at the level of the Djohar medical analysis laboratory in the Tlagh region and the applied microbiology laboratory within the Faculty of Nature and Life Sciences of Sidi Bel Abbes. The results show that the positivity rate of the examined ECBUs was 30%. The mean age of the patients was 50.60 years with a predominance of women. Urinary tract infection affects all age groups, with the most affected age group over 50 years old. The most isolated species are in decreasing order of frequency: *Staphylococcus spp* (91%), *Klebsiella spp* (9%). The strains isolated from *Klebsiella spp* are resistant to 100% amoxicillin, followed by a resistance to cefazolin of 57%, Imipenem, amikacin, gentamicin and ciprofloxacin are active on these strains with a sensitivity rate of 15%, 6 %, 27%, 42% respectively. Strains isolated from *Staphylococcus spp* are resistant to amoxicillin, Penicillin G, tetracycline by 75% followed by resistance to Tobramycin by 60%, Chloramphenicol, Fosfomycin, Gentamycin, Ciprofloxacin and are active on these strains with a sensitivity rate of 50%, 40%, 30% respectively.

INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial infections and is a major public health issue. (Zahir H. *et al*, 2019). The urinary tract infections frequency is estimated at 150 millions cases per year worldwide, (Bertholom C., 2016). They consist of the second reason for consultation in infectious pathology after respiratory infections, and the leading cause of nosocomial infection (nearly 50%).

Also the main reasons for microbiological testing and antibiotic prescription, Which increases the cost of treatments and bacterial resistance development (Zahir H. *et al.*, 2019). The urine cytobacteriological examination (UCBE) remains the key examination for the positive diagnosis of this infection, it allows to identify the responsible germ and to study its sensitivity to antibiotics. The isolation of the microorganism responsible for UI, reveals that the Gram-positive coccus, the Gram-negative bacilli (BGN), especially Enterobacteriaceae microorganisms are the most implicated germs in these infections (Bouguenoun, 2017). These bacteria occupy an important place in human pathology and constitute more than 80% of the germs isolated in the laboratory of medical biology. The frequency and severity of community or nosocomial infections for which these bacteria may be responsible (sepsis, nosocomial infections, meningitis, etc.), reflect management difficulties mainly linked to their resistance to antibiotics (Frasca D. *et al.*, 2008). The sample collection, as well as its route to the laboratory, must be carried out in strict conditions and in a well-defined protocol to avoid interpretation errors. The emergence of multiresistant bacteria (BMR) involved in the IUs limit the choice of antibiotics, hence the importance of adequate bacteriology documentation and adapted antibiotic therapy (Pavese P, 2003). The French-language infectious pathology company (Spilf) revised in 2015. The recommendations for the management of this pathology, in the permanent objective of limiting the development of antibiotic resistors, adapting to bacterial epidemiology. The objective of this work is to determine the bacteriological profile of urinary infection in the region of Tlagh, and follow the sensitivity profile to the antibiotics of uropathogenic bacteria, in a context of modification of the epidemiology of antibiotic resistance. According to our knowledge in Algeria, there is a problem of resistance to antibiotics in patients with urinary tract infections.

MATERIALS AND METHODS

a-Presentation of the Study:

This is a prospective, descriptive and analytical study carried out at the level of the Djohar private medical analysis laboratory at the level of the Telagh region (Latitude: 34.7849, Longitude: -0.573177, 34° 47′ 6″ North, 0° 34′ 23″ West), Sidi Bel Abbes and thus the applied microbiology laboratory within the biology department, Faculties of Natural and Life Sciences. Our study was carried out over a period of six months, from February 2021 to July 2021.

b-Inclusion Criterion:

Our study focused on any urine sample from a hospital department for a cytobacteriological examination of urine that is positive after 48 hours of hospitalization.

c- Exclusion Criteria:

We excluded from the study:

-Any urine sample from an outpatient.

-Any positive cytobacteriological examination of urine (ECBU) within a period of fewer than 48 hours.

-Any urine for which we have the same strain with the same antibiogram for the same patient

d-Data Collection:

We used an operating sheet containing:

-Application number, surname, first name, IP, gender.

-The cytological and bacteriological characteristics of urine.

-The antibiogram sheet

e-Bacteriological Analysis of Urine:

 e.1.Urine Chemistry:

e.1.1. The Urine Strip (US):

It is a tab with several squares of blotting paper impregnated with reagents that change color according to the presence of certain components in the urine. The strip should be soaked in

freshly emitted urine, in a clean but not necessarily sterile container.

Technical:

First homogenize the urine correctly by turning the cup slowly, several times, then immerse the strip 1 second (maximum) in the urine by fully moistening all the reactive areas. Never pour urine with a pipette on the strip, after draining quickly bypassing the slice of the strip on a paper towel to remove excess urine, finally turn on the stopwatch.

Procedure:

The US is a plastic rod on which reagents are placed that react to the various components present in the urine.

To test a urine sample:

-Urine should be fresh and collected in a clean, dry container;

-The sample is not centrifuged;

-The single-use strip is briefly soaked in urine, ensuring that all blocks are covered with urine,

The edge of the strip is pressed against the neck of the container to remove excess urine;

-The strip is then in a horizontal position for a while, which can range from 30 s to 2 min;

-The color of the test areas is compared to that of the color. The strip is held close to the pallet and carefully examined, then discarded.

Limitations of the US:

This method should not be used in patients surveyed, patients with a neurological bladder with chronic leukocyturia and in the case of certain drug treatments interfering with the reactivity of tests. The use of US is indicated when the clinical picture is discreet or atypical, but it must be followed by an ECBU. In terms of health savings, the use of the US would reduce the number of ECBUs carried out by a third. The test strips detect the leukocyte esterase produced by neutrophils in the urine. The sensitivity threshold is 104 leukocytes/ml

-Nitrites that testify to the presence of bacteria, mainly enterobacteria, which express a nitrate reductase capable of transforming nitrates into nitrites. The detection threshold for nitrites is quite high, corresponding very approximately to 10^5 colony-forming units (CFUs) ml (lower on some US). This explains why nitrites may be absent in the case of low bacteriuria.

e. 2. Cytobacteriological Examination of Urine:

e.2.1. The Arrangements for Levying:

-**Sampling Conditions**:

In practice, urine collection is most often done in cooperative adults by natural means according to the so-called "jet medium" technique and according to strict rules that condition the quality of the ECBU.

a) Cooperative adult subject: in a woman who has even minimal discharge, the implementation of vaginal protection is essential. The first part of urination will be rejected, allowing to eliminate all or part of the commensal flora of the lower urethra, and only the middle of the jet will be collected in a sterile vial (Saadoun M, 2020).

b) Non-cooperative or incontinent adult subject: the collection in women will be carried out by urinary probing using a small-caliber probe. This maneuver is to be avoided in humans because it provides prostatitis and it is preferred the collection by a penile collector, or even by catheterization above-published in case of urine retention (Saadoun M., 2020).

c) Information accompanying the sampling: this information is essential because it will allow the microbiologist to optimize the interpretation of the ECBU. They concern the age and sex of the patient, the mode and time of collection, the reasons for the request, the history of ITU, the notion of concomitant disease, the treatment possibly already instituted

(Saadoun M., 2020).

Best Sampling Time:

The sample is done in the morning because the urine is concentrated (dilution artificially decreases the count of microorganisms) and the bacteria have had time to grow during the night (more sensitive examination)

In men and boys: urine from the second stream is collected sterile after cleaning the urinary meatus.

In the girl: the sample is preceded by a careful perineal toilet made from front to back to avoid fecal contamination with several compresses moistened with saline (three compresses used for a single passage and discard one after the other), the sample is collected in a sterile vial, preferably in the middle of urine stream, during normal urination, without probing, the examination should be performed outside the menstrual periods.

In infants: after cleaning the perineal area and local disinfection, a collector is placed with an adhesive.

In the patient surveyed: urine is taken from the probe with a 5ml syringe, the use of an antiseptic reduces the number of microorganisms.

Preservation of Urine:

In order to avoid bacterial proliferation, transport to the laboratory must be fast in less than 2 hours. Beyond this time, urine can be stored at +4°C for 24 hours.

Receipt of Samples:

Urine is received in plastic jars, transparent, hermetically sealed and sterile.

The jar should be labeled to indicate the patient's first and last name.

e.2.2. Implementation of ECBU:

A cytobacteriological Examination of Urine Is Characterized by A Quantitative and Qualitative Analysis of Urine and Culture:

2.2. a.Macroscopic Study:

Urine is normally light yellow and clear. The emission of cloudy urine suggests a urinary tract infection, but is not specific; it can be related to the presence of crystals, drugs, etc.

In Particular:

Its appearance:

- Flaky deposit: Streptococcus.

-Glalar deposit: Group D fecal streptococci.

- Homogeneous disorder: Staphylococcus+

-Silky wave disorder: *Escherichia Coli*.

- Disorder due to the presence of mineral elements (phosphates).

- Its color: In the normal state the urine can have a light-yellow color, this is the case of polyuria (diluted urine) or dark amber yellow in case of fasting (concentrated urine).

As it can have a tint in case of a pathology:

-Orange-yellow in the case of acute febrile diseases,

-Red in case of presence of blood or haemoglobin or food pigments (red cabbage, beetroot) or after absorption of certain phenol-based medicinal products,

- Greenish brown in the case of hepatovesicular disease (presence of bile pigments),

-Black: a case of a malignant tumor such as melanosarcoma, or alcaptonuria (congenital enzyme anomaly),

-Brown turning red, after addition of alkaline and taking of certain plants,

- Blue, when taking methylene blue or during abundant intestinal putrefactions.

The smell: Urine has a characteristic smell that is difficult to define, due to the presence of volatile compounds at very low doses. This smell can be modified by adding odors to certain foods (for example asparagus, cabbage, radishes).

In some diseases, highly odorous volatile products may appear in the urine, such as ketone odor in the case of diabetes.

e.2.2.b. Microscopic Study:

(a) Fresh Examination:

Performed on a urine sample homogenized on a Vortex type agitator. This examination makes it possible to visualize and list the figurative elements of the urine using a calibrated hematometer or "Malassez cell". The Kova slide system is

a plastic blade that has the advantage of being disposable and containing 10 cells of 1 mm3 per blade. The result is expressed in elements per mm3, or per ml.

The elements visualized are:

-Leukocytes and red blood cells

Normal urine contains less than 104 leukocytes and 103 red blood cells/mm3.

-Cylinders

The cylinders originate from renal tubular light. They can be hyaline, physiological. Pathological cylinders contain red blood cells and/or leukocytes (hematic and/or leukocyte cylinders), their presence makes it possible to identify the kidney as the source of hematuria and/or leukocytes.

Crystals: Can be medicated, calcium oxalate, uric acid, or phosphoammoniaco-magnesium. The latter sign the presence of lithiasis secondary to an infection related to a urea-producing bacterium (including Proteus mirabilis, Corynebacterium urealyticum) and which causes alkalinization of urine (Saadoun M, 2020).

Pathogens:

Presence of Bacteria:

(b) **Direct Examination After Colouring**:

Direct examination, after Gram staining, of non-centrifuged urine shows a sensitivity close to 100% only for bacterial concentrations

> 105 CFU/ml. Despite its sensitivity, this examination remains essential by providing immediate information to the clinician on the type of bacteria involved. In case of the presence of a polymorphic flora, the direct examination will make it possible to evoke contamination of the sample and to immediately have another analysis carried out.

e.2.2.c. Uroculture:

The vast majority of bacteria responsible for urinary tract infections are not demanding and are grown on ordinary agars: CLED agar, sometimes a chromogenic medium Uri SELECT is added or agar to the blood.

Seeding:

Seeding must meet the dual purpose of enumerating bacteria and isolating the bacteria involved by obtaining colonies that are distinct from each other.

Calibrated Handle Method:

This method is currently the most widely used. The urine is collected using a loop of 10 µ l and seeded according to a standardized method that allows, thanks to an abacus, to convert the appearance of the culture into CFU / ml.

Incubation of urocultures: The majority of bacteria in urinary tract infections grow in 18 to 24 hours and, outside of particular contexts, there is no need to prolong incubation.

Except in the case of demanding, deficient bacteria, or negative culture, despite the presence of bacteria on direct examination, it is necessary to modify the culture medium (blood agar or "chocolate"), and the atmosphere (anaerobic and CO_2) and prolong the incubation.

Disadvantages of the Calibrated Handle Method:

In the case of the use of a calibrated handle made of platinum wire, the volume delivered by it must be regularly checked (Evans Blue calibration curve). Indeed, after a large number of uses, the calibration of the handle can be modified (corrosion, sterilization of the material).

Interpretation of Urocultures:

The Kas criteria that serve as a reference for the interpretation of bacteriuria are as follows.

The thresholds of bacteriuria, during the culture, are defined according to the clinic and the bacterium found:

-10^3 CFU/ml for acute cystitis with E. coli, Proteus spp, Klebsiella spp, and S. saprophyticus.

-10^5 CFU / ml for cystitis to other bacteria (especially enterococcus).

-10^4 CFU/ml for pyelonephritis and

prostatitis (Saadoun M, 2020).

Antibiogram:

The antibiogram consists of determining the sensitivity and resistance to antibiotics of a bacterium isolated in a sample, and supposed to be at the origin of an infectious process (Saadoun M, 2020).

The choice of antibiotics is varied according to the family of bacteria, the lists of ATBs to be tested are standardized by the European Committee and the French Society of Microbiology- the Antibiogram (EUCAST/CA-SFM) (Saadoun M., 2020).

The reading of the antibiogram is done after incubation, inhibition zones of variable diameters appear around a few disks, the results are compared to the critical values of the tables of the antibiogram committee of the French society:

-Sensitive (S): if the inhibition diameter is less than the diameter of the critical concentration.

-Intermediate (I): the inhibition diameter (corresponding to the MIC) greater than the diameter of the critical concentration.

-Resistant (R): if the inhibition diameter is between the diameters of critical concentrations (Saadoun M., 2020).

Dissemination Methods: The standard antibiogram by diffusion in agar medium

A blotting paper pellet containing a certain amount of antibiotics is deposited on the surface of agar. The antibiotic diffuses around the disc which creates a gradient of homogeneous concentration decreasing from the edge of the pellet to the outside. After seeding the agar by the bacterium to be tested, the growth of the agar occurs all around the disc, stopping to form a halo of growth inhibition at the place where the concentration of the gradient in the agar is equal to the minimum inhibitory concentration. It follows that the only measurable tangible parameter is the diameter of this inhibition halo. It is therefore necessary to transform this diameter into "S", "I" or "R" to give the clinician useful information in the choice

of antibiotic therapy (Saadoun M, 2020).

Bacterial Identification:

The identification of an unknown bacterial strain is done by the comparative study of its characteristics with the characteristics of reference strains, defined and listed in such a way as to assimilate by comparison to a species already known and classified.

Identification is necessarily done on a pure culture. This condition is essential to eliminate the presence of any contaminant that would distort the analysis.

- **Macroscopic Identification:**

Macroscopic examination of cultures is the first examination carried out from isolation after incubation. The appearance of the colonies depends on the medium used (Streptococcus, for example, gives larger colonies on blood agar than on ordinary media), the duration and the temperature of incubation.Colony descriptions should include several elements: size, shape, surface appearance, opacity, consistency, and colour

Microscopic Identification:

- **Gram Staining**:

This is the reference coloring in bacteriology. It makes it possible to highlight the properties of the bacterial wall and to use its properties to distinguish between Gram-positive and Gram-negative bacteria (Gram-negative bacteria have a thinner wall than Gram-positive ones and moreover they are rich in lipids (the outer membrane of the wall). This is because Gram-negative bacteria appear pink while Gram-positive bacteria appear purple.

e.2.2.d. Biochemical Identification:

Depending on the morphological aspect of the bacterial colonies, the morphology of the bacteria after staining, their growth characteristics (respiratory type, cultural requirements, etc.), their pigmentation, their smell, of their hemolytic character on blood agar, the bacteriologist focuses on a bacterial family or a bacterial genus in particular.

If necessary, it supplements its

presumption of the bacterial genus by orientation tests (respiratory type, catalase and oxidase). Nevertheless, accurate identifications of bacterial species use, for the most common bacteria of medical interest, biochemical identification galleries that are manual or can be read on automated systems.

A number of basic biochemical assays are used in the development of bacterial strain identification galleries.

After recalling the orientation tests (respiratory type, catalase and oxidase), a number of metabolic tests will be detailed. These main concerns are carbohydrate metabolism, protein metabolism and lipid metabolism. Agglutination tests complement bacterial identification in some cases.

f.1. **Study of Respiratory Modes:**

Three respiratory enzymes are commonly sought.

-**Catalase Search:**

Principle: Catalase is an enzyme found in most strict aerobic and optional anaerobic bacteria. It breaks down hydrogen peroxide (H_2O_2) from oxidative respiration into water and oxygen that is released.

$$2H_2O_2 \longrightarrow 2H_2O_2 + O_2$$

This test is often performed for differentiation between staphylococci and streptococci (Marchal bourdon JL, Richard C, 1982).

- **Oxidase Search:**

Principle. It is an enzyme that intervenes in various redox couples, the enzyme sought is phenylene-diamine-oxidase (Delarras, 2007).

-**Search for Nitrate Reductase:**

Some bacteria can use carbohydrates in anaerobic in the presence of a hydrogen acceptor which can be the NO- ion. They then have a special enzyme: nitrate reductase which catalyzes the reaction of nitrates (NO2) and possibly nitrogen (N2).

$$NO3- \rightarrow NO2- \rightarrow N2$$

Technique: A tube of nitrated broth (nutritious broth supplement of 1.5% potassium nitrate) is seeded with the bacterium studied, then it is incubated at 37 ° C for 18 to 24 hours.

After incubation is added 3 drops of sulphanilic reagent + acetic acid (nitrate1) and 3 drops of alpha-naphthylamine reagent + acetic acid (nitrate2) (Frenry et al., 2008).

Reading

A red coloration means that there is the presence of NO2 →nitrate reductase + no staining is added zinc powder:

-Red staining: zinc powder reduces nitrates to nitrites → negative nitrate reductase

-No staining means a positive nitrate reductase.

f.2. Study of Carbohydrate Metabolism:

¬ Study of the different sugars

• **TSI (Tri Sugar Iron)**

This complex makes it possible to confirm the fermentation of glucose with or without gas production and to guide the germ identity by studying the attack on sucrose, lactose and the production of H_2. The fermentation of sugars leads to the production of acids causing the pH indicator, which is phenol red, to turn yellow. (Marchal bourdon JL, richard C, 1982).

Study of Mannitol Degradation (mobility mannitol test):

Principle: The mannitol mobility medium makes it possible to detect the fermentation of mannitol and the mobility of the germ to be studied.

-**Carbohydrate Attack Route:**

Principle: Carbohydrate-using bacteria follow two metabolic pathways: an oxidative pathway in the presence of oxygen from the air and a fermentative pathway in the absence of oxygen from the air (Ferron, 1984).

Study of Mannitol Degradation (mobility mannitol test):

Principle: The mannitol mobility medium

makes it possible to detect the fermentation of mannitol and the mobility of the germ to be studied.

Determination of the Fermentation Pathway:

The identification of the fermentation route taken by a germ is very important for its diagnosis. It consists in differentiating between the two pathways of fermentation of mixed acids highlighted by the RM test (methyl red) and the butandiol pathway highlighted by the Voges Proskauer (VP) reaction. (Marchal bourdon JL, richard C, 1982).

Enzymes Involved in The Breakdown Of Sugars:

Principle: The most commonly sought-after enzyme is beta-galactosidase, which is responsible for the breakdown of lactose.

Orthonitropyphenyl-B-Dgalactopyranoside (ONPG) is a structural analogue of lactose. This colourless synthetic substrate can be degraded to galactose and orthonitrophenol (yellow soluble compound).

Technique: A dense bacterial suspension is prepared. The reaction is all the faster the more bacteria, therefore more enzymes.

We add an ONPG disk. We incubate at 37 ° C for 24 hours.

Reading: A positive reaction: yellow coloration →presence of a beta-galactosidase.

A negative reaction: no yellow coloration → absence of beta-galactosidase.

f.3 Study of Protein Metabolism:

a. Search for Decarboxylases:

Principle: Three decarboxylases are frequently sought: lysine decarboxylase (LDC), ornithine decarboxylase (ODC) and arginine dihydrolase (ADH).

When bacteria possess these enzymes, they will metabolize amino acids in amine format (Schaeffer AG, 1990).

Technique: Using a pure culture of three tubes of broths containing the amino acid to be studied, a small amount of glucose and bromocrezol purple are seeded, hence the purple coloration of the medium (Schaeffer AG, 1990).

Reading: After 6 pm at 37°C, a cloudy purple medium corresponds to a positive reaction. A yellow medium corresponds to a negative reaction.

b. Tryptophan Research:

Principle: Tryptophan is an enzyme that breaks down tryptophan into indole.

Technique:

- Dissolve 16.0 g of dehydrated medium (BK163) in 1 liter of distilled or demineralized water.

-Shake slowly until completely dissolved.

- Divide into tubes, at the rate of 3 to 5 ml per tube.

-Sterilize with an autoclave at 121°C for 15 minutes.

- For the identification of Escherichia coli, transfer a typical culture use obtained from selective agar into a tube of medium so prepared or ready-to-use medium. employment (BM076).

- Incubate at (44.0 ± 0.5) °C in a thermostat bath for (21 ± 3) hours in the case of compliance with NF EN ISO 9308-1.

- Incubate at 37°C for 24 hours.

Reading: The red coloration on the surface (red ring) indicates indole production and that the indole bacterium is positive (Schaeffer AG, 1990).

f.4. Use of different carbon sources

a-Use of Citrate as the Only Source Of Carbon:

Principle: The absence of a red ring on the surface indicates that bacterialindole is negative. This medium (simmon citrate) contains only one source of carbon (citrate) plus pH indicator (bromothymol blue). Bacteria possess a citrate permease are able to use citrate by inducing a 1st alkalinization of the medium. (Marchal bourdon JL, richard C, 1982).

Technique: Half of the slope is seeded, the upper part will serve as a negative control and this from a culture always coming from an agar medium, incubation at 35 ° C for 18 hours (Marchal bourdon JL, Richard C, 1982).

Reading: The degradation of citrate results in a mid-shift from green to blue. Turn of the indicator to blue → positive citrate bacteria.

Unchanged medium: bacteria do not have permease necessary for the use of citrate →bacterium citrate negative.

Table 1: Identification using the classical gallery.

Test	Technique	Reading
Oxidase test (Flandroits et Chomarat, 1998)	Spread part of the colony on the oxidase disc using a sterile buttoned Pasteur pipette.	A positive reaction results in a purple coloration in a few seconds, which highlights the colorless reduced form of methyl derivatives of paraphenylene diamine, in their purplish-pink semiquinone oxidized form.
Catalase test (Reiner, K, 2010)	A colony is taken from the petri dish and placed on a blade. A drop of H2O2 is poured on this colony	Positive reactions are manifested by immediate effervescence (bubble formation).
VP and RM Test (Meziani M, 2012 ; Leulmi ZK, 2015)	Seed the Clarck and Lubs medium with the bacterial strain. After incubating at 37 ° C for 18 hours. Divide the medium into two tubes, for the RM test add 2 to 3 drops of methyl red. And for the VP add a few drops of the VP1 reagent and the same volume of the VP2 reagent.	The reading of this medium allows the study of the glucose fermentation pathway. The RM test consists in highlighting the fermentation pathway of mixed acids which consists in assessing the pH of the medium after 24 hours of culture ; The VP test consists in highlighting the acetoin produced by butanedolic fermentation, by a reaction colored pink after 15 min
Urea indolore test (Meziani M, 2012)	We seed the environment 'urea-induole' directly to from the colonies of K. pneumoniae using a loop Platinum. After incubation at 37°C for 24 hours. The middle is divided into two tubes. One can look for the indole production by Kovacs reagents and the TDA is revealed by the addition of iron perchloride.	Urease is highlighted by a changé in coloration of the middle to pink, and production of the indole translates into a ringred on the surface after adding Kovacs, while tryptophan-deaminase detected by the appearance of a brown color after the addition of iron perchloride.
TSI Test (Marchal bourdon JL, richard C, 1982)	It consists of sowing in Tight streaks the slope of the agar then by central bite the base, the reading is done after 18 hours of incubation at 37 ° C	Gas production translates into the formation of gas bubbles in the mass of the cap. The fermentation of glucose and/or sucrose results in the turning yellow of the mass of the Nerve. Thé production of H2S results in the blackening of the medium.
Citrate medium of Simmons (Solbi, 2013)	The seeding is done by means of a platinum handle by transverse streaks of the slope, the reading is done after 24 hours of incubation at 37 ° C.	The seeding is done by means of a platinum handle by transverse streaks of the slope, the reading is done after 24 hours of incubation at 37 ° C.

Biochemical Gallery API 20E:

The API 20E gallery, marketed by the bio company Mérieux, is a miniaturized, ready-to-use and standardized system.

The gallery has 20 microtubes containing dehydrated substrates. Below each tube, an acronym indicates the nature of the test. The tubes are seeded with a bacterial suspension made of physiological water (medium suspension medium. The reactions produced during the incubation period result in spontaneous colored turns or are revealed by the addition of reagents.

A bottom and a lid complete the gallery and make it possible to constitute an incubation box. The API 20 E gallery allows you to perform the following tests: ONPG, ADH, LDC, ODC, Simmons citrate (CTT), hydrogen sulphide production by thiosulfate reduction (H2S), urease synthesis (URE), search for a tryptophan deaminase (TDA), search for painless power (IND), acetoine production (VP), synthesis of gelatin (GEL), search for acidification of nine "lucids»: glucose (GLU), The gallery also allows the search for nitrate reductase which is done in the microbe "GLU" (Rahal, 2005).

RESULTS

Urine Chemistry:

The interpretation of the

colorimetric changes at the reactive zones is done by comparing the ranges with the colorimetric scale arranged on the vial containing the strips (Table2).

It is an orientation examination characterized by a good negative predictive value (NPV)> 95% in women and a good negative predictive value (NPV)> 90% in men (Cariou et *al.*, 2016; Koeijers J.J. et *al.*, 2007). The use of the urine dipstick alone (determination of the number of leukocytes and nitrites) (Bertholom C., 2016). A strip is said to be "negative" if it shows neither leukocytes nor nitrites. In women, in the absence of severe immunosuppression, a negative BU has a very good negative predictive value. In men, a negative BU does not rule out the diagnosis. The strip is positive if it detects nitrites and/or leukocytes. In women, a positive BU is sufficient for the diagnosis of uncomplicated acute cystitis. In men, a positive BU supports the diagnosis of urinary tract infection but must be confirmed by an ECBU.

B) Isolation of a strain: Our study focused on 2 strains of Staphylococci and Klebsiella collected at the medical analysis laboratory of Djohar, Telagh, SBA and applied microbiology laboratory within the biology department during a period from February 02 until July 2021.

Table 2: Urine strip results according to parameters.

Parameters	RESULTS	Values
Leukocytes	+	15
Nitrites	-	0
Urobilinogen	-	0,2
Protein	-	0
pH	+	6
Blood	-	0
Specific Gravit	-	1
ketone	-	0,1
Bilirubin	-	0
Glucose	-	0

Macroscopic examination of ECBU:

Urine gross examination results showed in table 3.

Table 3: Urine gross examination result.

Aspect	Color	Sediment
Clear and limpid	Yellow	Brick red

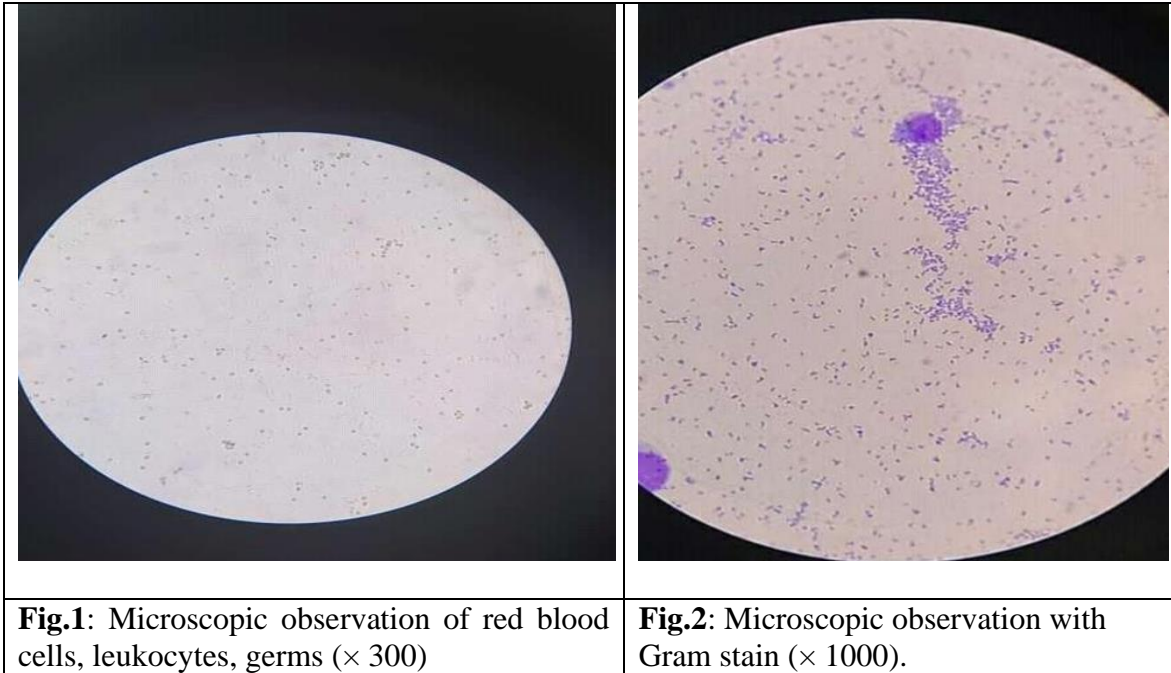**ECBU   Cytobacteriological Examination:**

During the observation of urine under the microscope, we noticed the presence of different elements such as leukocytes, red blood cells, germs (Fig.1).

The presence of leukocyturia and bacteriuria, as well as hematuria in large numbers, led us to a urinary tract infection. The presence of bacteriuria without leukocyturia is observed in an early stage of infection, a delayed inflammatory reaction, colonization after urinary catheterization, or in the case of an immunocompromised person. Also, leukocyturia without bacteriuria is encountered if the bacterial count is $<10^5$ CFU / ml, in the following cases: the presence of stones or foreign bodies in the urinary tract, irritation linked to the presence of a catheter, an infection non-bacterial or by viable non-cultivable bacteria, a urinary tract tumor, prior antibiotic treatment (decapitated infection) or in the case of diseases of the renal system (eg nephropathy).

Fresh microscopic observation showed short, immobile cocci. After Gram staining of a smear, carried out from a purified culture, showed that the strains obtained (at the objective x100) appear in the form of cockles or diplococci stained in pink. So these are Gram-positive cocci (Fig. 2).

| **Fig.1**: Microscopic observation of red blood cells, leukocytes, germs ($\times$ 300) | **Fig.2**: Microscopic observation with Gram stain ($\times$ 1000). |

Uroculture:

The macroscopic appearance of the isolates of *klebsiella spp* and *Staphylococcus spp* are shown in figures 3, 4.

Bacterial Count:

A count less than or equal to 10^4 CFU / mL most often corresponds to contamination, and therefore the absence of a urinary tract infection. However, such a result should be interpreted according to the leukocyturia and the clinical context (symptoms, taking antibiotics, pregnancy, the presence of a risk factor such as urinary catheterization or an intervention on the urinary tract). However, a count greater than or equal to 10^5 CFU / mL probably corresponds to an infection, provided that the sample was taken correctly. Urinary tract infections are most often monomicrobial.

In the case of bi microbial urine, two possibilities are to be considered: the presence of a germ of pathological significance and of a contaminant generally originating from the skin, vaginal or intestinal flora; or the presence of two pathologically significant germs,

often a second ECBU will make it possible to decide: If one germ is largely in the majority, it is likely that the second is a Contaminant; and if the two germs are in equal proportion, bi microbial infection is most likely.

In the case of polymicrobial urine, an ECBU must be redone on another sample, this is a sign of contamination. Bacteriuria without leukocyturia can be seen in the following cases: pregnant woman, immunocompromised, diabetic and infant.

Bacteriuria between 10^3 and 10^5 CFU / ml may be due to diluted urine, slow-growing bacteria, or ongoing antibiotic treatment. Confirmation will be done on a second sample. Observation of the incubated dishes shows that there is a typical appearance of the colonies of Staphylococcus and Klebsiella. The table below recapitulates the main characters of the colonies observed (Table 4).

Characters of *Klebsiella spp* and *Staphylococcus spp* Colonies

The main characters of *Klebsiella spp* and *Staphylococcus spp* colonies on Chromagar medium are shown in Table 5.

Fig.3: Macroscopic appearance of *Klebsiella spp* isolates on chromagar culture medium incubated at 37 ° C for 18 to 24 hours

Fig.4: Macroscopic appearance of *Staphylococcus spp* isolates on chromagar culture medium incubated at 37 ° C for 18 to 24 hours.

Table 4: Bacterial count.

Bacterial count CFU / ml	Leukocyturia	Interpretation
N<10 3	-	No infection
N< 103	+	Decapitated infection Fastidious bacterial infection
103< N<105	+/-	Questionable sample
N >105 Mono bactérienne	+/-	Urinary tract infection
N >105 Polybacterial culture	+/-	Contaminated sample

Table 5: Main characters of *Klebsiella spp* and *Staphylococcus spp* colonies on Chromagar medium

Environment	Strains	Form	Aspect	Opacity	Contour	Color
Chromagar	Klebsiella	Round, Domed	Mucous	Opaque	Regular, irregular	Metallic blue
	Staphylococcus	Domed	Smooth	Opaque	Regular	Golden

Antibiogram:

Each bacteria have its own antibiotic treatment (Figs. 5&6). The treatment of *klebsiella spp* with antibiotics are Ampicillin, Vancomycin, Amoxicillin, Amikacin, Gentamycin, Cefotaxime, Spiramycin, Tetracycline, Nalidixic Acid, Amoxicilin Clavulanic Acid, Chloramosphomycin, Ciprofloxamycin, Oxacosphomycin, Kanosphomycin, Oxacosphomycin, Cefotaxime, Spiramycin, Tetracycline, Nalidixic Acid, Amoxicilin Clavulanic Acid, Chloramosphomycin, Ciprofloxamycin,

Oxacosphomycin, Oxacosphomycin, Cefotaxime, Spiramycin, Tetracycline, Nalidixic Acid, Amoxicilin Clavulanic Acid, Chloramosphomycin, Ciprofloxamycin, Oxacosphomycin.

In this study: Amikacin and Nalidixic Acid and Ciprofloxacin and Fosphomycin (sensitive) Gentamycin, Spiramycin (intermediate). The others (resistant).

The treatment of Staphylococcus spp with antibiotics are Vancomycin, Amoxicillin, Amikacin Spiramycin, Tetracycline, Nalidixic Acid, Amoxicilin Clavulanic Acid, Chloramphenicol, Fosphomycin, Riphampycin, Oxacillin, Penicillin, Acidixicidixic Acid, Amoxicilin Clavulanic Acid, Chloramphenicol, Fosphomycin, Riphampycin, Oxacillin, Penicillin, Acidicillin, Tobycidicin, Tobycidicin, Tobycidixic Acid In this study: Gentamycin Fosphomycin, Riphampycin, Amoxicilin Clavulanic Acid, Chloramphenicol (susceptible) Tetracycline (intermediate). The others (resistant).

Fig.5: Effect of antibiotics on *Klebsiella spp* on Mueller-Hinton culture medium incubated at 37 ° C for 18 to 24 hours.
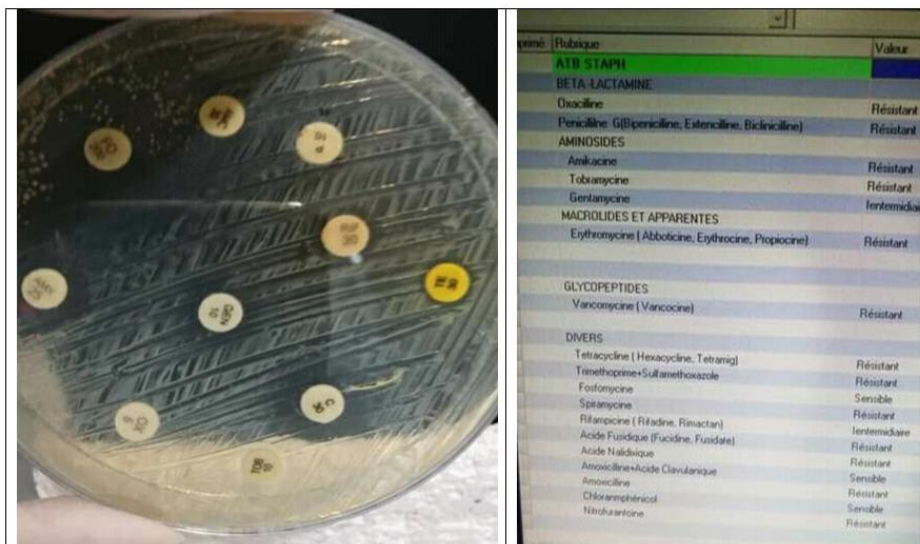

Fig.6: Effect of antibiotics on *Staphylococcus spp* on Mueller-Hinton culture medium incubated at 37 ° C for 18 to 24 hours.

Biochemical Identification:
Catalase Test:

Staphylococcus cells obtained degrade hydrogen peroxide (H_2O_2) and release air bubbles on the surface of their colonies (Fig.7) which means that this isolate is catalase-positive.

Oxidase Test:

The Staphylococcus bacteria do not possess a cytochrome oxidase which normally results in contact with N, N-dimethyl-1,4-phenylene diamine dichloride in 20 to 60 seconds, by the appearance of a red color rapidly turning into a very dark purple. This isolate obtained is, therefore, oxidase negative (Fig.8).

Fig.7: demonstration of catalase on two strains inoculated from chromagar culture medium incubated at 37 ° C for 18 to 24 H

Fig .8: demonstration of oxidase on two strains isolated from each other from chromagar culture medium incubated at 37 ° C for 18 to 24 hours.

Mannitol Mobility Test:

The color change of mannitol from red to yellow affirmed its fermentation by staphylococcus spp and *Klebsiella spp,* the appearance of the clear halos surrounding black showed its mobility. Mobility results in diffusion from the seeding line, however, immobile bacteria only grow along with the bite seeding. this method is not very sensitive because certain strains which are not very mobile may appear immobile. So this isolate is mannitol mobility positive (Fig. 9).

D) Frequency of urinary tract infections the cytobacteriological examination of urine is the main examination performed at the Djohar Analysis Laboratory in Telagh, SBA and Applied Microbiology Laboratory within the Faculty of Nature and Life Science. On the 21 samples taken, we find that the rate of negative cases (70%) is clearly higher than that of positive cases (30%), (Table 6).

In most cases, this is due to the over-prescribing of antibiotics before the diagnosis is substantiated. It is, therefore, a decapitated infection: - Either by self-medication before consulting the doctor, - Either initiated by the doctor early before carrying out the cytobacteriological study of the urine, The methylene blue stain, which in these cases shows a lymphocyte-type or mixed immune response, which means that the infection is either viral or parasitic. It can also be a urinary tract infection decapitated by the early intake of antibiotics, which results in sterile cultures.

Fig. 9: demonstration of mannitol on two strains isolated from chromagar culture medium incubated at 37 ° C for 18 to 24 H

Table 6: Breakdown of ECBUs carried out during the study period.

	Number	Frequency %
Positive ECBU	9	30%
Negative ECBU	12	70%
Total	21	100%

Characteristics of the study population:
Gender: Our study population is dominated by the female sex (Fig.10).
2 Age:

In women, the frequency of urinary tract infections increases with age. But two periods are prone to infections, one at the onset of sexual activity and the other in the postmenopausal period. In men, urinary tract infections increase from the age of 50, when prostate problems start (Table7).
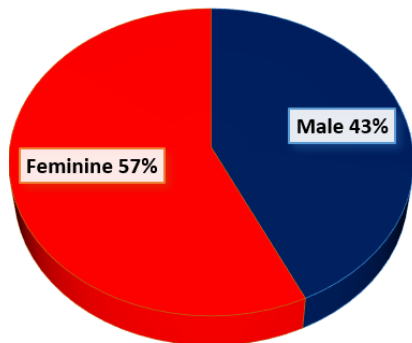

Fig.10: Distribution of patients having contracted a UTI by sex.

Table 7: Distribution of urinary tract infection by age

Age	ECBU -	ECBU +
Over 50 years	33,33%	66,67%
Under 50 years	60%	40%

According to Gram:
Gram-positive bacteria dominated the profile of bacteria responsible for urinary tract infection, Gram-negative bacteria were also found in 9% of cases (Fig.11).
According to the Germs Isolated:
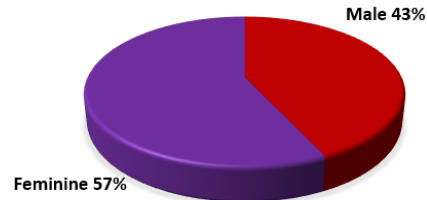91 % of the germs isolated are *Staphylocoques spp* while *Klebsiella spp* represents 9% (Table 8).

Fig. 11: Distribution of uropathogenic germs according to the type of GRAM.

Table 8: Distribution of UI according to the strains isolated.

Antibiogram	Workforce	Proportion in %
Staphylocoques spp	25	91
Klebsiella spp	4	9
Total	29	100

E) Antibiotic Resistance Profile:
The resistance of the germs isolated to antibiotics is determined from the results of the antibiogram after a period of 18 to 24 hours and 37 ° C on 9 samples are carried out in the Djohar medical analysis laboratory in Telagh and in the applied microbiology laboratory in the faculty of nature and life science in Sidi Bel Abbes.
All strains isolated from *Klebsiella spp* are resistant to 100% amoxicillin, followed by

57% resistance to cefazolin, Imipenem, amikacin gentamicin and ciprofloxacin are very active on these strains with a sensitivity rate of 15%, 6%, 27%, 42% respectively, (Fig.12).

All strains of Staphylococcus spp

are resistant to amoxicillin, Penicillin G,

Tetracycline 75% followed by Tobramycin resistance 60%, Chloramphenicol, Fosfomycin Ciprofloxacin and are very active on these strains with a sensitivity rate of 50%, 40%, 30% respectively, (Fig.13).

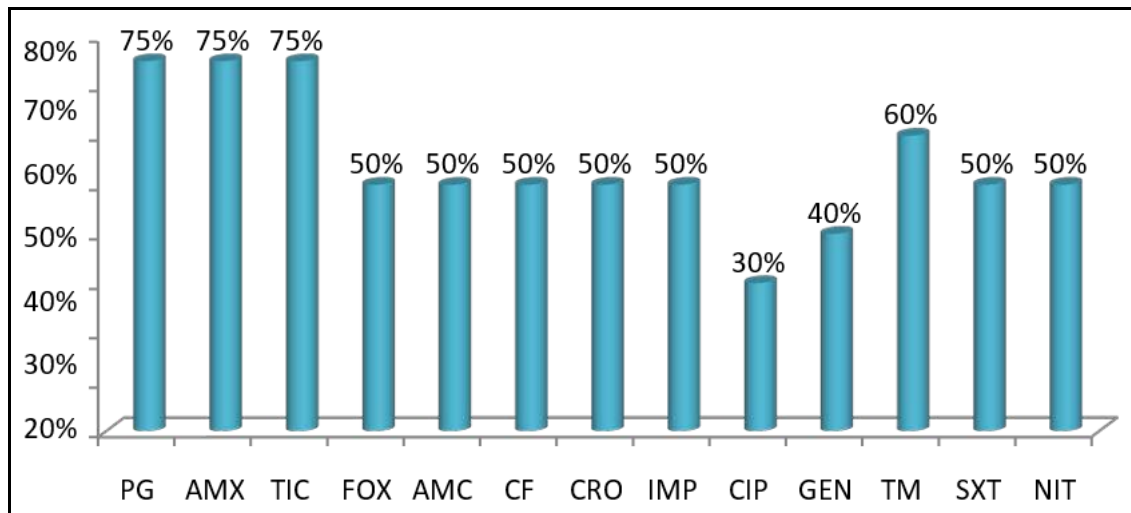**Fig.12**: Resistance profile of Klebsiella spp.

Fig.**13:** Resistance Profile of *Staphylococcus spp*

DISCUSSION

The profile of local and up-to-date bacteriological data is essential for the effective application of the new consensuses in the management of this pathology, in particular the prescribing of first-line antibiotic therapy effective against uropathogenic bacteria. This presence of leukocytes and nitrites in patients makes it possible to suspect the presence of the germs responsible for a urinary tract infection. According to Helene et *al*. (2007) affirm that the negativity of the two parameters leukocytes - nitrites has an excellent negative predictive value (97.5%), that is

to say, that when these two parameters are negative, we have 97.5% of "Chances" of not being in the presence of infected urine.

When urine is infected, in almost 90% of cases, we observe the positivity of at least one of the two preceding parameters. But the positivity of one of these two parameters does not confirm the infection (the positive predictive value of the test is poor: 39.7%) and should lead to the performance of an ECBU. This simple strategy saves both patient, physician and lab time and money.

However, this BU test requires proper interpretation with knowledge of false positives and false negatives, knowing that this is a colorimetric test with visual reading; and that only one screening test remains for children to perform ECBU, especially in an outpatient setting. It should in no case alone, lead to the diagnosis of UI or lead to antibiotic therapy (Helene *et al.*, 2007).

The causes of false negatives are summarized; False negatives at the BU: In the absence of nitrites; Bacteria that do not express nitrate reductase: Staphylococcus saprophyticus, Streptococci and enterococci, Acinetobacter -Low bacteriuria, urinary pH, Diuretic acid and diluted urine, Male urinary tract infections. In the absence of leukocytes: Immunosuppression, neutropenia -Male urinary tract infections.

Cytobacterioligical urine exam; The ECBU is the only test that confirms the diagnosis of UTIs, by identifying the type of bacteria involved and by studying its sensitivity to antibiotics (antibiogram). It imposes rigorous sampling techniques, precise conservation and production conditions as well as a critical interpretation of the results.

Epidemiology of urinary tract infections; The frequency of UTIs varies by country and is influenced by different risk factors. This study covers all the bacteria isolated from urine samples received at the Djohar analysis laboratory, Telagh.SBA and applied microbiology laboratory within the nature and life science faculty in Sidi Bel Abbes. Among the ECBUs which reached our laboratory during the period concerned, the positivity rate of the examined ECBUs was 30%. This frequency is high compared to that found at the level of the microbiology laboratory of the CHU of Marrakech 2015 where the rate recorded was 12.26% (Benhiba I *et al.*, 2015); as well as that recorded at the Ibn Sina University Hospital in 2012 where the rate recorded was 23.27% (Elharch I, 2013); in Mauritania 18.4% (Hailaji N.S.M. *et al.*, 2016) and in Tunisia, the frequency was 15.44% (Ben Haj Khalifa A., Khedher M., 2010).

Distribution by sex Among; the 30% positive ECBUs, we found that 43% of patients were male and 57% female. a sex ratio F / M = 1.3. which agrees with the data in the literature, both national and international: a sex ratio F / M of about 1 .6 in a study carried out in Mauritania 2016 (Hailaji N.S.M. et *al.*, 2016) 1.12 at the Marrakech University Hospital 2015 (Benhiba I et *al.*, 2015) and 1, 7 for the study conducted at MEKNES Hospital 2012 (Hazi Filali F, 2012)

Women are much more prone to UTIs than men, which may be explained by the anatomy of the urethra which is short, wide, close to the perianal area. The urethral meatus and the peri-urethral skin are frequently colonized by germs of digestive origin. During urination, there are marginal updrafts that promote the migration of germs to the bladder. In women, the urethra can undergo subtle trauma during sexual intercourse that promotes the entry of germs (Richet *et al.*, 1988). The prescription of estrogen-progestogen treatments, an imbalance of the saprophytic bacterial flora of the vagina and urethra secondary to too much hygiene, a sexually transmitted infection,

or on the contrary anorectal colonization by poor hygiene, is also favored by sexual intercourse which facilitates the passage of germs normally present in the vagina into the bladder. • The use of spermicidal diaphragm gel is also a contributing factor (Bléry M. *et al.*, 2006; Hooton T.M. e*t al.*, 1996; Daniel J. *et al.*,2003; Kunin C.M., 1994).

Leotard S., Negrin N. (2010) reported a predominance of women. This female predominance is also confirmed by (Ilyass ES- Saoudy 2019) who found a frequency of UTIs of 52% in women and by (CISSE F., 2019) who found a frequency of UTIs of 65, 5% in women. While the study by Mohammed Sbiti *et al.* (2017) shows a male predominance of urinary tract infections with EBLSE s, others have reported. These differences may reflect regional disparities in antibiotic prescribing practices related to gender, the nature of patient recruitment in a hospital, and also may be the result of methodological biases such as inclusion criteria (prostate surgery, etc. .).

Distribution by age; Analysis of the frequency of urinary tract infections shows that this infection affects all age groups. Our study corroborates that age appears to be a risk factor in the incidence of urinary tract infections. People over 50: The most affected age group is that of patients over the age of 50. Elderly people have multiple reasons for developing UTIs such as decreased immune response, bladder capacity, glycosuria, increased prostate size, decreased secretions, chronic diseases (diabetes). Numerous studies confirm that among the risk factors for UTIs by a multi-resistant bacterium (BMR) including EBLSE, is advanced age, generally over 65 years (Ait miloud KH, 2011). According to Tiouit D. et *al.* (2001) out of 1369 positive ECBUs in the Maghreb, the frequency of urinary tract infections increased in diabetics, the immunocompromised, probe carriers as well as in bedridden people. In women, menopause increases the risk of contracting a urinary tract infection, according to Pechere *et al* (2017); UTIs may be more frequent due to the absence of certain hormones after menopause), (Taale A. *et al.*, 2017). People under the age of 10 also represent a large percentage of UTIs, mainly patients with urinary tract malformations. Indeed, vesicoureteral reflux is the main malformation of the ureterovesical system sought during a first episode of urinary tract infection in children (El Kharrat *et al.*, 2007). For people aged between 20 and 30 and between 30 and 40 years old the age group between 20 and 30 years old represents 19% of those infected. That between 30 and 40 years old represents 18%. These age groups represent that of adults. Most of these are pregnant women or others who are sexually active. Indeed, pregnancy modifies the immune defenses, causes anatomical modifications which are the dilations of the urinary tract, a hormonal imbalance (increase in secretion) and chemical modifications (glycosuria, increase in urinary pH, increase in the concentration of amino acids). The importance of urinary tract infections in women belonging to the adult category can be explained by anatomical and physiological factors specifically favoring the installation of pathogens (short urethra, pregnancy, etc.)

People in the age groups 10 to 20 and 40 to 50: People aged 10 to 20 and 40 to 50 have the lowest percentages of 3% and 5% respectively. Indeed, According to Vorkauffer *et al,* in 2011, the frequency of urinary tract infections increases with age, which explains the low percentage of people aged between 10 and 20 years, because they are young people with strong immune defenses. The low percentage of people aged between 40 and 50 can be explained by the fact that, in women, two periods are conducive to infections, one at the start of sexual activity and the other in the postmenopausal period. In men, urinary tract infections increase from the age of 50, at the time of onset of prostate

disorders (Vorkauffer *et al.*, 2011). These two situations exclude people between the ages of 40 and 50 (Vorkauffer S., 2011).

Antibiotic resistance rate of Klebsiella strains All the strains isolated from Klebsiella are resistant to 100% amoxicillin, followed by a resistance to cefazolin of 57%, Imipenem, amikacin, gentamicin and ciprofloxacin are very active on these strains with a sensitivity rate of 15%, 6%, 27%, 42%. According to Mohamed Vall (2015), the frequency of resistance of Klebsiella is 100% with amoxicillin, this result corresponds to the result found in our study, but it is more important than those noted by Minouche *et al.* 2010 and Toutou Sissoko *et al.* (2006) reporting a percentage of 64% and 93.3% respectively. Amoxcillin-clavulanic acid resistance rate was reported in a 2016 study in Constantine (53%), however, Hlaiji reports 35% resistance to this antibiotic (Lacheheub L, Bendagha Y, 2016; Hailaji N. S *et al.*, 2016). For gentamycin and ciprofloxacin, our results are not similar to those found by Toutou Sissoko *et al.*, 2006 who found a rate of 64.8 % for Gentamycin and 56% for Ciprofloxacin. (Toutou Sissoko M, 2006; Mohamed Vall R., 2015). Antibiotic resistance rate of Staphylococcus strains All strains isolated from Staphylococcus are resistant to amoxicillin, Penicillin G, tetracycline of 75% followed by resistance to Tobramycin of 60%, Chloramphenicol, Fosfomycin, Gentamycin, Ciprofloxacin and are very active on these strains with a rate of susceptibility 50%, 40%, 30%. This result is explained by the fact that currently, more than 90% of S. aureus strains are resistant to penicillin G by the production of penicillinase (Saadoun M, 2020). The genetic support for this resistance was described by Pinho et al., The penicillinase gene belongs to a transposon, most often located on a large plasmid, which can also carry genes for resistance to other antibiotics

(aminoglycosides, macrolides) and antiseptics (Pinho MG, 2001) A study carried out at the HMIMV in Rabat showed resistance of 39.1% to tetracycline and 15% to rifampicin. These results are also in agreement with those reported in other studies carried out in Africa. (Lacheheub L, Bendagha Y, 2016; Hailaji N S *et al.*, 2016; Kesah C *et al.*, 2003). On the other hand, the emergence of UTIs among hospitalized patients has been favored by a number of factors such as: - The massive use of antibiotics favoring the selection of the most resistant bacteria; - Cross-transmission through healthcare workers promoting the spread of bacteria resistant to ATB. Overall, we also note that the bacterial strains of the Telagh region of Sidi Bel Abbes have acquired some resistance to antibiotics and that health practitioners have significantly changed the antibiotic therapy prescribed to patients with urinary tract infections. Bacteria modify their behavior in the presence of the antibiotic in several ways, direct and continuous contact is among the factors that increase bacterial resistance. In addition, we cite the case of environmental conditions and the change in the lifestyle of men who are in direct contact with antibiotics that have changed the sensitization of bacteria vis-à-vis these drugs (consumption of meat, milk, water).

CONCLUSION

This phenomenon of multi-resistance to antibiotics is a major public health problem in Algeria, worrying and alarming because of the potential risks (increased morbidity and mortality, additional economic costs and installation of highly resistant bacteria in hospital services). Better control in terms of strict compliance with hygiene measures, isolation of carriers, reasoned use of antibiotics and defining therapeutic and prophylactic strategies adapted to local epidemiology are the key actions to slow down their emergence and dissemination.

We insist on developing a more reliable approach to enable health laboratories to strengthen surveillance, which must be continuous and systematic.

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