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URINARY TRACT INFECTIONS BY ENTEROBACTERIA IN NEWBORNS AND CHILDREN PEDIATRICS EL MANSOURA, CONSTANTINE, ALGERIA.

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INTRODUCTION

The urinary tract infection is one of the most common serious bacterial infections in infants and children (Abiodium et al., 2007). Urinary tract infection (UTI) is often associated with functional or anatomic abnormality of the urinary tract, the most common of which is vesico - ureteral reflux (Yves et al., 2009).

The urinary tract is a common source of infection for infants, toddlers and children. Urinary tract infections are important because they can cause acute or long-term morbidity as hypertension or decreased renal function (Girardin, 2008). The prevalence of IU depends on many factors including age and sex, but it is in the first year of life that the incidence of the first episode is the highest. Signs and symptoms of UTIs are often nonspecific, particularly in neonates and infants. The diagnosis is based on urine cytology testing (urinalysis), which imposes strict conditions of collection, storage and execution.

In terms of microbiology, Enterobacteriaceae represent 82.4% of urinary isolates. Extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL) is a serious problem in health care facilities. Despite measures taken to prevent their dissemination, an increase of their number is noted (Lahlou et al., 2010).

The purpose of this work is the isolation, identification and study of the sensitivity profile of the causative organism in these urinary tract infections in newborns and children of the Pediatric Hospital El Mansoura of Constantine.

MATERIAL AND METHODS

This is a prospective study which was carried out for a period of two months (10 March to 09 May 2014) at the Unit of Bacteriology, Pediatrics of El Mansoura Constantine.

1 - Sample and inclusion criteria

Urine samples were examined during the study period. Each urine sample was routinely analyzed.

During this period, we collected all non-redundant strains isolated from hospitalized patients or external consultants in pediatric El Mansoura Constantine.

Microbiological criteria of urinary infection are selected: a leukocyte count greater than or equal to10^4 cells/ml and greater than or equal to bacteriuria 10^5 CFU / ml.

2 - Identification of bacteria

It was carried out by conventional bacteriological characteristics (cultural, biochemical .....).

3-The study of the sensitivity to antibiotics

Performed by using normal flood antibiotic agar from disks according to the standards of the Committee on Antimicrobial Sensitivity of the French Association for Microbiology (CA-SFM). 14 antibiotics were tested in this study.

-As penicillins: amoxicillin (AMX), amoxicillin + clavulanic acid (AMC), ticarcillin (TIC), piperacillin (PIP).

-Cephalosporins: cefazolin (CZ), cefotaxime (CTX) The carbapenems. Imipenem (IMP). Aminoglycosides: gentamicin (GN), amikacin (AN).

-The fluoroquinolones pefloxacin (PEF).

-Sulfonamides: sulfamethaxazole + trimethoprim (SXT).

-Polymixins: colistin (CS)

-Nitrofurans: nitrofurantoin (FT)

-Phenicols: chloramphenicol (C).

RESULTS

During the period of our study which lasted from 10/01/2013 to 03/09/2013, 155 cytobacteriological urinalyses were performed in the service of Bacteriology of the Pediatric and Pediatric surgery Hospital EL Mansoura - Constantine. In 155 urine culture media, 31 strains were collected including 13 external and 18 in hospitals.

1 Distribution of strains according to the units

The distribution of strains according to origin shows that 48% of strains are isolated from the outside (non-hospital strains), against 52% isolated from different departments of the hospital (hospital strains). The service records of infants the greatest rate of stem with a frequency of 26%, followed by the big kid with a frequency of 10% services; however the lower distribution is recorded in intensive care unit 0%. (Table1).

Table 1: Distribution of strains according to the services: Nb=31

Services	Infected cases	Percentage %
NRS	8	26%
GE	3	10%
CHIR	2	7%
REA	0	0%
TA	15	48%
CTX	2	6%
HDJ	1	3%
Total	31	100%

NRS : infant, **GE :** big kid, **CHIR :** surgery, **REA :** ressuscitation, **TA : outpatient treatment**, **HDJ :** day hospital, **CTX** : infectious service.

2 Distribution of strains by gender

Out of 31isolates: 78% are girls and 22% are boys, a sex ratio of 1.58. (Table 2).

Table 2: Distribution of strains according to sex: Nb=31

Sex	Infected cases Nb=31	Percentage%
Girls	19	78%
Boys	12	22%

3/Division of strains according to age

The highest number of patients meets the range from 1 month to 4 years (80%). The range from 4 to 14 years identifies older hospitalized children (20%).

4 / Distribution of germs isolated from urinary tract infections in children

Enterobacteriaceae are a total of 87% of the found germs. *E.coli* is well ahead in isolated urinary tract infections in children with 55% of bacteria, followed by respectively 16% *K. pneumoniae* and *Proteus mirabilis.*

Table 6: Distribution of seeds isolated from urinary tract infections for children: Nb=31

Isolated germs	Infected cases Nb=31	Percentage %
E.coli	17	54,83%
K.pneumoniae	5	16,12%
Proteus mirabilis	5	16,12%
Pseudomonas aeroginosa	1	3,22%
Entérocoque	1	3,22%
Yeast	2	6 ,45%
Total strains isolated	31	100%
Enterobacteria	27	87%
BGN	28	90,32%
BGP	1	6%

Enterobacteria : (*E.coli , K.pneumoniae, Proteus mirabilis)*

BGN : Gram negative bacilli (*E.coli , K.pneumoniae*, *Proteus mirabilis , Pseudomonas aeroginosa* **. BGP** : Gram positive bacilli (*Enterococcus*)

5-Antibiotic resistance

5-1 - Profile of overall resistance of isolated Enterobacteriaceae

The table below shows that the resistance of isolated Enterobacteriaceae is high for amoxicillin (AMX), amoxicillin + ac.clavulanique (CMA), ticarcillin (TIC), piperacillin (PIP), cefazolin (CZ) Sulfamethoxazole and Trimethoprim (STX).

In contrast, a low resistance to amikacin (AN), pefloxacin (PEF) and colistin (CS) is recorded. Moderate resistance to gentamycin (GM), Chloramphenicol (C), and nitrofurantoin (FT). (Table 4).

Table 4: Overall resistance profile of enterobacteria : Nb=27

Antibiotics	Number resistant strains	Percentage%	Number susceptible strains	Percentage%
AMX	**22**	**81.48%**	**5**	**18.52%**
AMC	**19**	**70.34%**	**8**	**29.63%**
TIC	**20**	**74.07%**	**7**	**25.93%**
PIP	**19**	**70.34%**	**8**	**18.52%**
CZ	**13**	**48.14%**	**14**	**51.86%**
CTX	**10**	**37.03%**	**17**	**62.97%**
IMP	**0**	**0%**	**27**	**100%**
GN	**7**	**26%**	**20**	**74%**
AN	**1**	**3.70%**	**26**	**96.3%**
PEF	**5**	**18.51**	**22**	**81.49**
CS	**5**	**18.51%**	**22**	**81.49%**
FT	**9**	**33.33%**	**19**	**66.67%**
STX	**12**	**44.44%**	**15**	**55.56%**
C	**8**	**29.69%**	**19**	**70.38%**

5-2 - Rate of ESBL among Enterobacteriaceae isolated

Among the 27 strains of Enterobacteriaceae isolated from urinary tract infections in infants and children, 10 ESBL-producing strains.

ESBL 6 belonging to the species *E. coli* isolated on 17, 3 to about *Klebsiella pneumoniae* 5 strains isolated, and about 1 ESBL on 5 *Proteus mirabilis* isolated.

5-3 Resistance profile of *E.coli* to antibiotics

Table 5: Resistance of *E.coli* to antibiotics: Nb=17

Antibiotics	**Numbers of bacteria resistant to antibiotics N=17**	**Percentage%**
AMX	11	64.70%
AMC	11	64.70%
TIC	11	64.70%
PIP	11	64.70%
CZ	6	35.2%
CTX	6	35.2%
IMP	0	0%
GM	2	11.76%
AN	0	0%
PEF	5	29.41%
CS	0	0%
FT	2	11.76%
STX	8	47.05%
C	1	5.88%

5-4 Resistance profile of *Klebsiella pneumoniae* to antibiotics

Table 6: **Resistance of *Klebsiella pneumoniae :* Nb=5**

Antibiotics	**Numbers of bacteria resistant to antibiotics N=5**	**Percentage %**
AMX	5	100%
AMC	4	80%
TIC	5	100%
PIP	4	80%
CZ	4	80%
CTX	3	60%
IMP	0	0%
GM	4	80%
AN	1	20%
PEF	0	0%
STX	4	80%
CS	0	0%
CHL	2	40%
FT	2	40%

Resistance profile of strains of *Proteus mirabilis* to antibiotics

Table 7 : Resistance strains of *Proteus mirabilis :* Nb=5

Antibiotics	**Numbers of bacteria resistant to antibiotics** **Nb=5**	**Percentage %**
AMX	**5**	**100%**
AMC	4	80%
TIC	4	80%
PIP	4	80%
CZ	3	60%
CTX	1	20%
IMP	0	0%
GM	1	20%
AN	0	0%
PEF	0	0%
STX	0	0%
CS	5	100%
C	3	60%
FT	5	100%

DISCUSSION

In our study, 31 strains were isolated from hospitalized patients and external consultants including 27 strains belonging to the Enterobacteriaceae. El-Mansoura pediatrics receives an average of 13 strains of Enterobacteriaceae per month.

Our study shows that urinary tract infections are more common among girls, 78% against 22% for boys, the results being consistent with the literature data (Guys, 2004; Belarmain, 2011). The sex of the child is considered as a criterion of infection caused by vesico-ureteral reflux (VUR), it is admitted that 30% of girls with UTI have reflux, and that 60-80% of them are a recurrence within 18 months following the first episode of infection. This could also explain the low incidence of urinary tract infection in boys, are the numbers of spontaneous reflux especially for high-grade boys who are very different from those found in girls (Gyus and Morrison-healing Lacombre , 2004).

Patient age has an influence on the frequency of urinary tract infections. We note that the section of 1 month to 4 years is the most affected among all children. This result is consistent with those reported by Benhalla in 2009 in a study carried out in Algiers indicating 97% of children hospitalized for urinary tract infections in infants. Our results are also consistent with those of Belermain Kongo in 2011, indicating that the range lower than or equivalent to 5 years of age is the most affected.

The influence of age is shown in the bladder maturation and consequently in the anti-vesico-ureteral reflux system. This maturation is typically possible until the age of 2 years. It shows an increase in the average length of the ureter within the bladder that rises from approximately 5 mm in the newborn to 13mm in average in adults.

Some circumstances also promote the emergence of a urinary tract infection in infants: diapers, immature bladder, the narrow and diarrhea foreskin, Pediatric poor hygiene, micturition disorder, vulvitis, constipation, pinworms… (Mohammedi, 2013).

In our study Enterobacteriaceae are the most frequently isolated bacteria from urinary tract infections in children with a percentage of 87% related to the strong position of the perineum colonization by these pathogens of digestive origin. *E.coli* is well ahead of the bacteria involved in the IU. The percentages of different Enterobacteriaceae are as follows: 54.53 % *E.coli* , 16.12% *Klebsiella pneumoniae*, 16.12% *Proteus mirabilis* . This distribution is similar to that recorded in pediatrics in Algiers with the following figures: 47.2% *E. coli*, *Klebsiella pneumoniae* 19.4% , 11% and *Proteus mirabilis* (Benhalla et al, 2009 .) . Urinary tract infection is generally upward because there is a strong perineal colonization by enterobacteria of digestive origin, especially E.coli (Alvarer et al. , 1992). Furthermore, there are specific uropathogenecity factors, *E.coli* have adhesins , *K. pneumoniae* and *Proteus mirabilis* secrete urease .

About antibiotic resistance, Enterobacteriaceae isolated in our study have high resistance to penicillins and cephalosporins. We note a frequency of 37.04% of β-lactamases-producing strains extended spectrum (ESBL) among isolated Enterobacteriaceae. The increasing antibiotic resistance of bacteria involved in the IU limits the choice of antibiotics in therapy. The ESBL-producing bacteria are also resistant to most antibiotics, except imipenem and amikacin which have an excellent activity. These results are similar to those reported in a Tunisian study (Hillier et al., 2010).

The emergence of resistance of the Enterobacteriaceae to quinolones and fluoroquinolones is the main problem related to their use. This resistance involves different mechanisms, the most common being the modification of targets (Tiger Heron et al., 2006).

Multiresistant *E. Coli* strains including cefotaxime is a serious problem in the countries of the eastern Mediterranean coast which reach 70% in Egypt (2007), and respectively 22% and 28% in Morocco (2007) and Turkey (2006) (www.infectiologie.org.tn / pdf / Lart / pdf).

Our results could be explained by the continuing increase in the incidence of ESBL-producing strains in El-Mansoura pediatrics Hospital in Constantine. This is likely the result of the selection pressure due to extensive use of β-lactams (Hammimes and Belaib, 2011).

Among the five strains of *Klebsiella pneumoniae* isolated, three ESBL producing a frequency of 60%, this result is similar to that reported by Sekhri-Arafa in 2011 indicating a frequency of 64% among 170 strains of isolated *Klebsiella pneumoniae*. Our ESBL also have strengths associated with the GN and SXT.

Proteus mirabilis is a ESBL-producing strain. These Strains have strong resistance to AMX, AMC, TIC and PIP. Our results are similar to those reported by (Leopold et al., 2009) indicating Cameroon, 80% AMX, AMC 50%, 55% TIC and PIP respectively. However the strength of 60% to 20% in CZ and CTX remains higher compared with that of a European study with 33.3% resistance CZ and 2.3% in the CTX (Honderlick et al., 2006). These

resistances are acquired as *Proteus mirabilis* is naturally sensitive to β-lactams and does not have the cephalosporin class C for the above aminoglycoside resistant strain to 20% in GN and 0% NA. This result is similar to that found in Tunisia for 427 strains of *Proteus mirabilis* where 19.5% resist GN and 2% in the NA.

CONCLUSION AND OUTLOOK

This study has allowed us to highlight the bacteria involved in UTIs in infants and children during the study period. Enterobacteriaceae are the most frequently isolated bacteria and are also strongly productive of ESBL. This is particularly worrying since cephalosporins are widely used in the IU, which increases the risk of ESBL acquisition.

E. coli remain the main bacteria responsible for UTI in infants and children. Strains resistant are frequently to antibiotics as well as *Klebsiella* and *Proteus*.

Whether the antibiotic is prescribed or not, support should be provided along with better detection and treatment of risk factors for infection and perineal hygiene adapted to avoid the repetition of infections.

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