Ambulatory management of urinary tract infections in children: experience of the pediatric medical emergency department in Rabat.

Abstract

The aim of the study is to describe the clinical epidemiological characteristics and bacteriological profile of UTIs in infants and children, to determine the main risk factors for the occurrence of UTIs, and to identify the causes of UTIs urinary tract infections, to compare the interest of CRP and let procalcitonin assays for the diagnosis of febrile urinary tract infections as well as the interest of imaging (renal scintigraphy and ultrasound of the urinary tree) in the diagnosis of febrile urinary tract infections. This observational study of a cohort of 169 patients (children aged more than 28 days, 119 girls and 40 boys) conducted in the pediatric emergency department of the children's hospital of the university hospital of Rabat over a period of 6 months.The diagnosis of UTIs is based on the detection of germs in the urine, either indirectly by urine dipstick or by urine culture. However, the interpretation of microbiological results can be tricky: an inappropriate urine collection technique, particularly in neonates and young children, is a pitfall that the clinician must take into account to avoid misdiagnosing UTI, usually by over-diagnosis.The location of high UTI involving the renal parenchyma or low UTI limited to the bladder, which determines the morbidity of the infection, the therapeutic management and the imaging work-up, remains a matter of debate. DMSA renal scintigraphy, the reference examination in the case of high UTI, cannot be recommended as a first-line examination because of its cost and the practical difficulties of performing it. Biological markers of inflammation (leucocytosis, CRP, procalcitonin) do not always allow the diagnosis of ANP to be made with certainty.

Keywords : Urinary tract infections, ambulatory management, bacterial infections, paediatrics, leukocyturia, bacteriuria, clinical epidemiological characteristics and bacteriological profile.

Introduction :

Urinary tract infection remains a public health problem and is one of the most frequent bacterial infections in paediatrics [1, 2]. It is characterised by the multiplication of micro-

organisms within the urinary tract, which is responsible for bacteriuria, accompanied by an inflammatory reaction with an influx of leukocytes in the urine: leukocyturia. Its prevalence in infants and children is 3-5% in girls and 1-2% in boys. By the age of seven, an estimated 7.8% of girls and 1.7% of boys have experienced at least one episode of UTI [3]. Its clinical presentation is variable, revealed by various pictures with a symptomatology all the more atypical as the child is younger [3-5], it is often associated with a vesico-urethral reflux or an obstructive uropathy, any urinary infection must be investigated, its essential risk is the occurrence of renal scars, sources of hypertension and renal failure [6]. The diagnosis is based on the detection of germs in the urine by the ECBU, the interpretation of whose microbiological results is sometimes delicate. The markers of inflammation (leucocytosis, CRP, procalcitonin) do not always allow the diagnosis of UTI. The diagnosis therefore remains a presumptive one, based on the association of a suggestive clinical picture and a biological inflammatory syndrome. The aim of our work is to describe the clinical epidemiological characteristics and bacteriological profile of UTIs in infants and children, to determine the main risk factors for the occurrence of UTIs, and to identify the causes of UTIs urinary tract infections, to compare the interest of CRP and let procalcitonin assays for the diagnosis of febrile urinary tract infections as well as the interest of imaging (renal scintigraphy and ultrasound of the urinary tree) in the diagnosis of febrile urinary tract infections .

Materials and methods.

This is a prospective observational study of a cohort of 169 patients conducted in the pediatric emergency department of the children's hospital of the university hospital of Rabat over a period of 6 months .

All children aged more than 28 days consulting the pediatric emergency department were included, for whom the diagnosis of a first episode of urinary tract infection was confirmed by cytobacteriological examination of the urine (leukocyturia > 10^4 and bacteriuritis > 10^5 associated with fever (temperature > 38°C).

Children with previously diagnosed malformative uropathy, previous urinary tract infection and severe sepsis were excluded.

Urine was collected after antiseptic perineal cleansing, in a sterile container in the middle of the stream in older children, or with a collection bag in children who had not yet acquired

daytime cleanliness. This bag was changed after further disinfection if the child had not urinated within 30 minutes.

The blood work-up included a haemogram, CRP, procalcitonin, blood count and renal function.

Renal ultrasound was performed to look for malformative uropathy responsible for UTI during the first week. The DMSA renal scan was performed on average on the seventh day.

Analyses of results: data entry was done by Excel and then analysed by SPSS 12.0 .

Quantitative data were expressed as means and standard deviations in the case of a Gaussian distribution and as median and quartiles in the case of a non-Gaussian distribution. Qualitative data were expressed as medians and quartiles.

We carried out a correlation study by a pearson test between the value of CRP and procalcitonin .

We evaluated the total cost of outpatient management and compared it to the cost of inpatient management.

Results:

Over the six-month period, 159 children were included in our study. Our patients were divided into 119 girls and 40 boys with a sex ratio of 0.34 in favour of girls. The mean age was 23 months with extremes of 1 month and 13 years (table 1). The clinical signs were variable and variously associated, of which the main ones, in addition to fever , were abdominal pain in 52 patients, diarrhea-vomiting in 49 patients and urinary burning in 44 patients. For factors favouring the occurrence of urinary tract infection, 62 patients (39%) had poor toilet training. Nappy wearing in 90 patients (56.6%), constipation in 18 patients (11.32%), oxyurosis in 14 patients (9%), 33 boys were uncircumcised (82.5%), dermatitis in 14 patients (11.32%), vulvovaginitis in 5 girls (4.2%), primary enuresis in 4 patients and phimosis in 1 patient. The ECBU culture found an Escherichia coli in 46 patients, Proteus mirabilis in 3 patients, staphylococcus in 3 patients, Klebsiella in seven patients (9.3%). The mean value of CRP in our patients was 76.8 mg/L (median = 74.47 mg/L) with extremes of 5 to 324 mg/L. It was found to be pathological (>20mg/L) in 100 patients or 63%. The mean

PCT value was 5.26 ng/mL (standard deviation = 14.8ng/mL) with extremes of 0.05 ng/mL to 28 ng/mL . The study of the correlation of CRP with procalcitonin in the diagnosis of febrile urinary tract infection revealed a positive correlation with r0= 0.73, this correlation is significant ($p<0.001$).

For radiological investigations, 159 ultrasound scans were performed and returned normal, as well as 159 DMSA scans which did not reveal any parenchymal lesions. Treatment was started as soon as the results of the direct examination were obtained, with a single antibiotic therapy based on a 3rd generation cephalosporin, initially by the parenteral route until apyrexia was maintained: for 2 days in 154 patients, 3 days in one patient and one day in 4 patients; then one day in 4 patients , then an oral relay with cefixime for a total duration of 14 days, the evolution under treatment was favourable.

The average cost of outpatient treatment was 135 $ compared to an average cost of 400 $ for inpatient treatment, a saving of 260 $ for an average hospital stay of 6 days.

Discussion:

UTI remains a common paediatric condition worldwide. It is one of the main reasons for consultation [7]. The frequency of UTIs varies according to the age and sex of the child [1, 8]. At pre-school age, girls are more often infected than boys, and by the age of six, 7% of girls and 2% of boys have suffered at least one episode of UTI [3, 10]. In our series, we found a predominance of urinary tract infection in the 1 to 24 month age group. With an incidence of 75% in the female sex. This is in line with observations in the literature [1, 9-12]. The proximity of the terminal digestive tract to the urogenital tract and the short urethra explain the predominance of UTI in the female sex. In addition, the vagina has commensal flora that can be pathogenic to the urinary tract [4, 13]. The clinical manifestations in our patients were polymorphous and variable according to age, dominated by fever, often isolated in infants, sometimes associated with abdominal pain, vomiting and diarrhoea, with a clinical picture that first suggested a digestive infection. Urinary signs become increasingly clear with age. In older children, the clinical presentation becomes more typical.

Enterobacteriaceae dominated the bacteriological profile of UTIs in our series, among which Escherichia coli was the most common bacterium involved with 85.18%, followed by Proteus mirabilis 5.55% and Klebsiella pneumoniae 1.85%. These results show the important role of

these 3 generations of enterobacteria in the etiology of UTI. This is also reported by several national [1, 12, 14] and international [2, 15-19] studies. In France Moulin & al [20] isolated 59% Escherichia coli, 8% Proteus mirabilis and 5.3% Klebsiella. While other authors have found Klebsiella to be the second most common pathogen of UTIs after E. coli [4]. The ascending pathophysiology of UTIs and the high colonisation of the perineum by enterobacteria of digestive origin, and in particular Escherichia coli, associated with specific uropathogenicity factors such as bacterial adhesins, explain this predominance [13, 21, 22].

There is currently no consensus and no prospective studies on the indications for imaging after the first episode of urinary tract infection in children [23]. Ultrasound is a simple, non-invasive and inexpensive examination, and is the examination of first resort in the acute phase, which allows the search for structural anomalies of the urinary tree, to specify the size of the kidneys and the corticomedullary differentiation, The European Association of Urology recommends ultrasound for any child with a first episode of febrile urinary tract infection [24], the American and Canadian societies recommend it only for infants under 2 with a first episode of febrile UTI [25, 26], while NICE recommends ultrasound only for infants under 6 months of age [27], in the face of an atypical urinary tract infection or one that is unresponsive to treatment. In our study all patients had an ultrasound scan, no abnormalities of the urinary tract were found.

PCT is a precursor protein of calcitonin without hormonal activity [17]. It is the earliest and most sensitive marker of inflammation. Studies have shown that PCT allows early diagnosis of bacterial infections, and it correlates with the severity of these infections; thus PCT can predict prognosis [18-20]. Normally, PCT does not increase in local bacterial infections unless the infection is accompanied by systemic inflammatory reactions [20-22]. Most authors have concluded that PCT has good diagnostic accuracy and clinical value in pyelonephritis, with sensitivity and specificity ranging from 0.5 to 1.0 [19] respectively from 70% to 100% and from 70% to 97% [23-28]. However, a Belgian team found a lower sensitivity and specificity (68% and 23%, respectively) with no obvious difference in threshold for population characteristics [29]. In our study only 80 out of 159 patients with a UTI had a positive procalcitonin (greater than or equal to 0.5 ng/ml) with a sensitivity of 66.8%.

CRP is a protein of inflammation and is produced in hepatocytes [28] . Its concentration increases 12 hours after a stimulus and doubles every eight hours to reach a serum peak between 36 and 48 hours [12,16]. It remains elevated if the inflammation persists and decreases rapidly upon resolution or after antibiotic treatment as it has a short half-life of four

to seven hours [29]. CRP remains a sensitive but unspecific marker for the diagnosis of ANP. In Bigot's study, its sensitivity was 93% but its specificity did not exceed 30% for a threshold value of 20 mg/l. In our study, its level was > 20 mg/l in 63% of the 159 children who received it.

The treatment of urinary tract infections in children has long been a source of debate on the choice of antibiotic, the route of administration and the duration of treatment, which in most cases depend on the clinical presentation but also on local and individual preferences [10]. third-generation cephalosporin as a first-line intravenous treatment and an aminoglycoside followed by an oral relay is recommended by French and German guidelines [27]. The recommendations of the American Academy of Pediatrics as well as those of the latest Cochrane review have shown that there is no evidence to support this recommendation.

They have also shown that there is no difference in the acute phase in terms of fever or at six months in terms of renal scarring whether the child is aged more than 1 month old and without underlying uropathy should be treated orally or parenterally [25, 30]. Intravenous antibiotic therapy is recommended if there are signs of sepsis or food intolerance [27][7,24]. Oral therapy should be considered as soon as the clinical condition improves [7,10]. The duration of treatment for ANP recommended by the American Academy of Pediatrics and the Canadian Paediatric Society is 7-14 days versus 7-10 days recommended by NICE [25, 27, 31]. In our study, patients received C3G monotherapy, initially intravenously until apyrexia was maintained and then orally. The total duration of treatment was 14 days. Apyrexia was achieved on the second day of IV treatment in 154 patients, on the first day in 4 patients, and after 3 days of treatment in one patient.

After a febrile UTI in children there is a risk of developing parenchymal scarring which can lead to varying degrees of impaired renal function and/or hypertension [32, 33], in the literature this risk varies widely from one publication to another, ranging from 8% [34] to 60% [35] and is dependent on several factors, however, in recent publications[36], the risk of scarring after a first UTI is low, partly due to early diagnosis and treatment. In a Korean study by Mi Mi Oh et al [38], the duration of fever before antibiotic treatment of ANP was 4.52 +- 2.00 days in children with kidney damage while it was 2.65 +- 1.93 days in those without damage with a significant difference. In the same work, using the ROC curve, the authors found that a fever duration greater than 2.5 days was associated with kidney damage with a sensitivity of 86.8% and a specificity of 60.4%. In our series, the mean duration of fever before treatment was at 3.75 days, all scans performed in our patients did not show renal

damage. Scars also depend on the virulence of the germs and the host response [39]. More recent studies have shown that renal scars may not be acquired but congenital [40, 41]. In these cases, the scars are not the consequences of inflammatory lesions but correspond to dysplasia and hypoplasia. These studies may explain the absence of parenchymal lesions in our sample: due to the exclusion of patients with known malformations, and the absence of congenital abnormalities on ultrasound of the urinary tree in all our patients,

The identification of renal scars is done by means of DMSA scintigraphy performed between 3 and 12 months after the UTI. However, DMSA scintigraphy has certain limitations. It is expensive, radiating and difficult to perform in small children who must remain immobile for ten to 20 minutes. The distinction between acute and chronic lesions is not always simple and there may be variations in interpretation between different observers [42]. Currently, several studies have shown that serum pct concentration at the time of UTI correlates with the presence of renal scarring [43, 44], and it can be used as a marker of choice to screen for patients with parenchymal involvement; a procalcitonin level greater than 0.5 ng/ml was predictive of parenchymal injury in 87-92% of febrile children with UTI [45]. PCT is less expensive than DMSA scintigraphy, is easily performed [46] and avoids patient irradiation. Its high sensitivity and excellent specificity make it the marker of choice for screening patients with parenchymal involvement. DMSA scintigraphy performed at a distance from the acute episode to assess possible sequelae, it could be reserved for patients whose PCT was increased in the acute period. At a time when some authors are proposing a reduction in the duration of intravenous antibiotic therapy [34, 47], PCT could be included in the patient selection criteria. Thus, patients with a normal PCT at the time of diagnosis could be offered oral antibiotic therapy more rapidly.

Conclusion:

Urinary tract infection (UTI) is a common condition in children with a variety of clinical presentations. E. coli is responsible for 70-90% of UTIs in children. The diagnosis of UTIs is based on the detection of germs in the urine, either indirectly by urine dipstick or by urine culture. However, the interpretation of microbiological results can be tricky: an inappropriate urine collection technique, particularly in neonates and young children, is a pitfall that the clinician must take into account to avoid misdiagnosing UTI, usually by over-diagnosis. The location of high UTI involving the renal parenchyma or low UTI limited to the bladder, which

determines the morbidity of the infection, the therapeutic management and the imaging work-up, remains a matter of debate. DMSA renal scintigraphy, the reference examination in the case of high UTI, cannot be recommended as a first-line examination because of its cost and the practical difficulties of performing it. Biological markers of inflammation (leucocytosis, CRP, procalcitonin) do not always allow the diagnosis of ANP to be made with certainty. The diagnosis of ANP therefore remains a presumptive diagnosis, based on the association of a suggestive clinical picture, which varies according to the age of the child, and a biological inflammatory syndrome.

Consent

As per international standard, parental written consent has been collected and preserved by the author(s).

Ethical Approval:

As per international standard or university standard guideline participant consent and ethical approval has been collected and preserved by the authors.

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Table 1: Distribution of patients by sex and age group

Sex **Age (months)**	**boys**	**girls**	**Total**	**%**
1 – 24	33	77	110	69,2
>24	7	42	49	30,8
Totale	40	119	159	100

Table 2: The main clinical signs.

Functional signs	**N=159**	**%**
Fever	131	82,4
Burning of the blader	44	27,7
dysuria	28	17 ,6
hematuria	11	6,9
pyuria	15	9,4
Abdominal pain	52	32,7
Diarrhoea	49	30,8
Deydratation	1	0.6

Anorexia	34	21,4
Vomiting	48	30,2
Irritability	16	10
Refusal to suckel	9	5,7
Hypotonia	9	5,7
drowsiness	8	5
Back pain	11	6,9

Figures

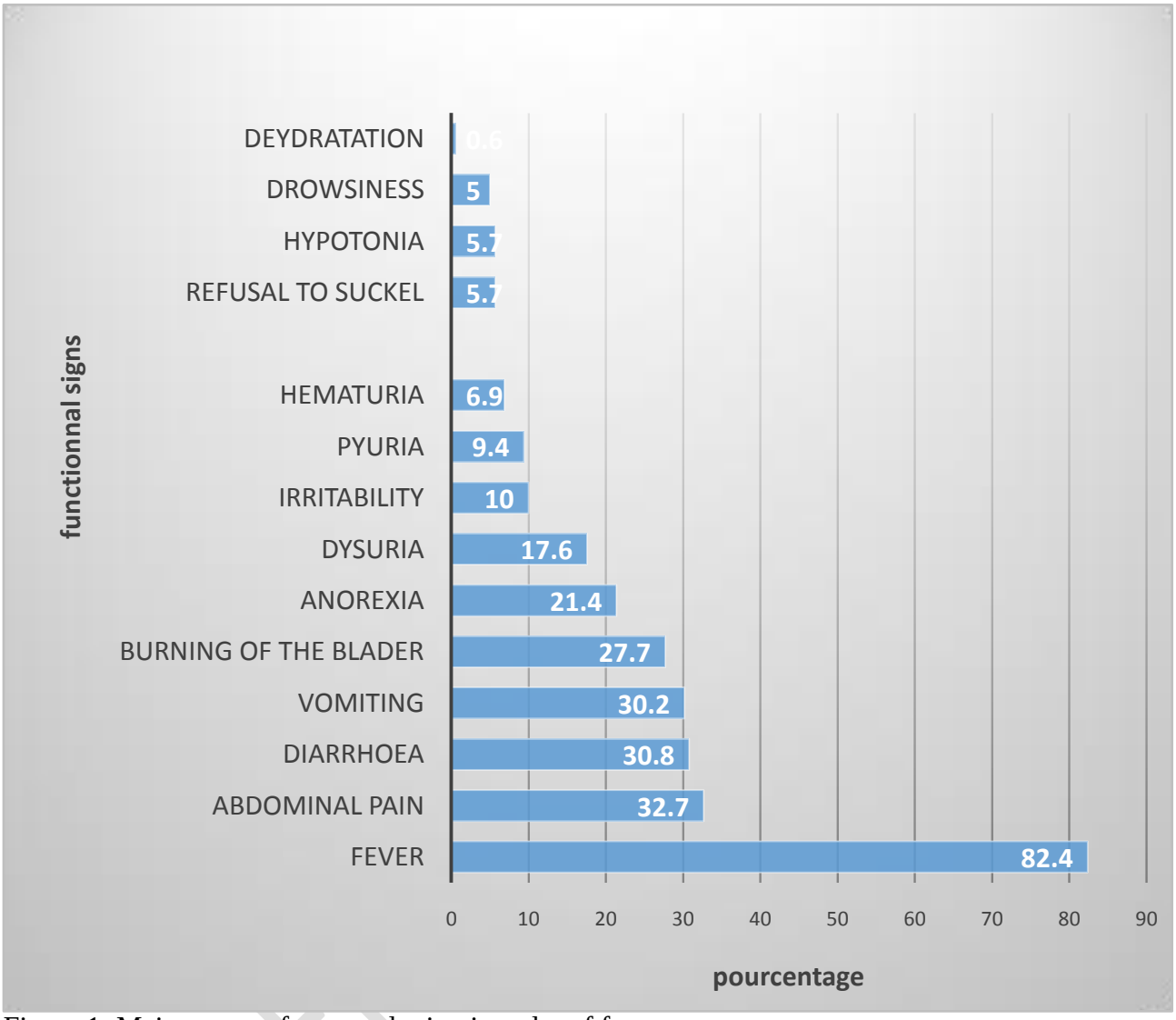

Figure 1: Main reasons for consultation in order of frequency.

Sex / Germ	boys	girls	N=54	%

1-negatif-gram :	***15***	***35***	***50***	***92,59***
enterobacteriaceae	15	35	50	92,59
E. coli	14	32	46	85,18
Klebsiella	-	1	1	1,85
Proteus mirabilis	1	2	3	5,55
2-positif-gram :	***2***	***2***	***4***	***7,4***
Staphylococus	1	2	3	5,55
Staphylocoque aureus	1	-	1	1,85

Table 3: Germs identified on cytobacteriological examination of urine.

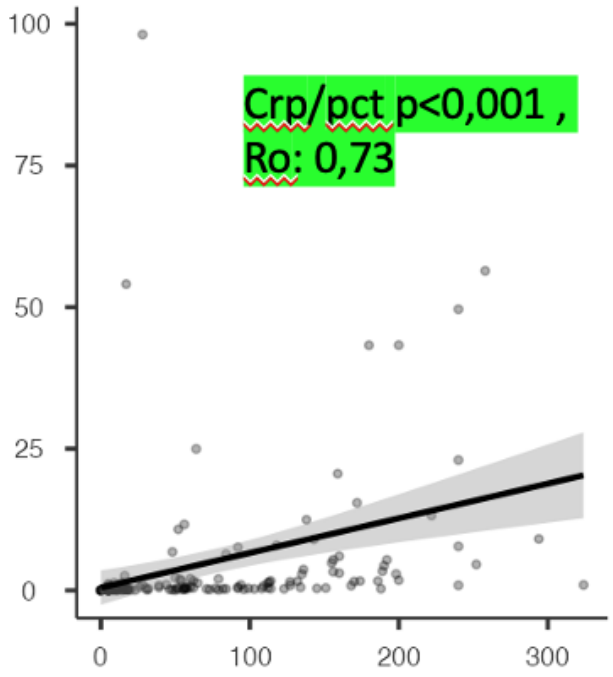

Figure 2: Concordance table between procalcitonin and CRP.

Benifit	cost	Cost of ambulatory care	Cost of hospital care	
Ultra sound	40	1	1	
ceftriaxone	6	2	6	
gentamicin	4	0	2	
Veinouse route	2	1	2	
consultation	10	2	2	
Daily consultation	6	0	6	
CBC	9	1	1	
CRP	10	1	1	
Day of hospitalisation	40			
total			135$	400$

Table 4 : Comparative table of costs between inpatient and outpatient care.