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## Challenges in Pediatric Urinary Tract Infection

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### Abstract

One of our aims is to assess the frequency of febrile urinary tract infection (UTI) in children aged one month to 12 years in a Lebanese sub urban region and to study its distribution in relation to gender and to the type of the episode whether it is an initial or recurrent attack. Another important aim is to study the association of UTI, in its initial or recurrent type with congenital renal anomalies detected by Investigation of upper and lower renal systems. Investigation is done by performing U/S of kidneys and bladder few days after diagnosis to visualize upper renal system then to perform VCUG after the end of treatment aiming to visualize the lower renal system. A third aim is to evaluate the yield of U/S and VCUG as investigating tools in the detection of renal anomalies associated with UTI. The results shows that 153 patients proved to have febrile UTI. The prevalence rate is 5.09%. Females constitute 112/153 (73%), while males count 41/153 (27%). Initial episodes are reported in 106 patients and recurrent episodes not previously investigated in 47 patients. 103 patients are investigated by performing U/S and VCUG that revealed 21 anomalies in males and 26 anomalies in females. (47/153) one third of all cases or 47/103 (45.6%) of investigated cases showed the presence of associated renal anomalies.

**Keywords:** UTI: urinary tract infection; U/S: sonography/ULTRASOUND ; VCUG: voiding cystouerthrography ; VUR: *vesicoureteral* reflux ; Pyuria: WBC in urine ; Bacteruria: bacteria in urine

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## **1. Introduction**

UTI is the most common serious bacterial infection in children because it is highly associated with long term sequelae as renal scarring, end stage renal failure and hypertension in adulthood.

The danger of UTI is mostly exerted in children less than 2 years whose kidneys are more prone to morbidity. By age 5 years, 8% of girls and 2% of boys must have had at least one episode of febrile UTI by age 7 (1). Besides, it is reported that renal parenchymal defects are identified in 3-15% of children within 1 -2 years of their first diagnosed UTI (2).

In another study it is reported that 10-15% of children develop renal scarring after their first febrile UTI (3). UTI is a marker to renal anomalies that may be easily missed so that the ongoing inflammatory process has a role in renal scarring. This is claimed by (NKUDIC), the National Kidney and Urology Diseases Information Clearing House (4). So, early diagnosis and management of UTI is very important and seems to be an easy task, but in fact it remains the most controversial issue in pediatrics (2). Investigating a first febrile UTI in children is changing with time, and it is reported that there is no ideal diagnostic imagery protocol to follow after a first febrile UTI (6). AAP guidelines to this imagery dramatically changed between 1999 and 2011. This shift is based on views that there is accumulation of evidence, casting doubt on the benefit of making a diagnosis of VUR and that data from the most recent six studies do not support use of antibiotic prophylaxis to prevent recurrent UTI with or without VUR grades 1-1V (9). The AAP 1999 guidelines claim that to investigate an initial febrile UTI, it is necessary to visualize both upper and lower renal systems by performing kidney and bladder U/S, then to do VCUG mainly in children 2 months – 2 years old. U/S must be done promptly to all children with febrile initial attack in the first few days of infection, then to perform either VCUG or RNC (Radionuclide Cystography) at the earliest convenient time (7). VCUG is the test of choice for detection and grading of VUR which is present in 25-40% of children with UTI. On the other hand, The 2011 AAP guidelines and the new guidelines of the National Institute for Health and Care Excellence (NICE) Aug 2007 have challenged their views towards a more selective approach concerning the investigation of the 1<sup>st</sup> febrile UTI episode(8)(9).The indication of U/S of kidneys and bladder is related to age of the patient, severity of infection and response to antimicrobials and that VCUG is not recommended as a routine measure but, done only if U/S reveals Hydronephrosis, scarring, high grade VUR or signs of Obstructive Uropathy as well as if recurrent UTI or complex atypical clinical circumstances are present . Besides, AAP guidelines 2011 claim that their recommendations are not exclusive and that variations from these guidelines may be appropriate (9) (10). This change brought confusion to clinicians who responded differently and the investigation of the first febrile UTI became a debatable issue. Besides, the AAP section of urology, claim that there is no sufficient evidence to change the current recommendations and they stressed the need to do both U/S and VCUG after first febrile UTI (6) (11) (12).

Based on all of this and considering the implementations of renal scarring and complications, we followed the routine procedure of performing U/S in the first few days of initial and recurrent not previously investigated febrile UTIs. A VCUG is then performed at the end of treatment to identify associated renal anomalies aiming to

study the close relation of UTI and congenital renal anomalies. Also The role of renal and bladder U/S and VCUG in detecting these renal anomalies are studied.

## **2. Materials and Methods**

Retrospective review of Files of 3050 admissions to a pediatric floor in a suburban hospital was done. These admissions covered a period of 2 years (2007-2009). 153 patients aged 1month to 12 years are found to have documented UTI. These patients are classified as an initial episode of febrile UTI or recurrent attack of UTI which was not investigated in their initial episode. Urine culture is considered positive when growing one single organism with colony count more than 100,000 per cubic ml of urine provided that urine is collected by a sterile procedure. Ways to collect urine samples varied between mid voiding stream sample, supra pubic aspiration and intravesicular catheter samples. Bag samples were not considered unless verified by suprapubic or catheter sampling. 103 cases are studied and investigated by doing U/S of kidneys and bladder in the first few days of infection followed by doing VCUG to detect associated congenital anomalies. Besides, the yield of U/S AND VCUG is discussed to estimate the renal anomalies that are associated with UTI. Cases of sepsis, asymptomatic bacteruria and UTI with previously diagnosed renal anomalies are excluded.

### **2.1 Selected Cases**

- Children presented in their in 1<sup>st</sup> febrile episode of UTI aged 1 month to 12 years old.
- Children presenting in a recurrent attack (second or more attacks) but were not initially investigated.
- All febrile patients with positive urine culture growing one organism > 100,000colonies per cu ml provided that urine is collected under sterile conditions.

### **2.2 Excluded cases**

- Documented sepsis
- Patients presenting with recurrent UTI and known to have renal anomalies or were free of anomalies on previous investigation
- Newborn < than one month old and children > 12 years old
- Children with immunodeficiency
- Children with asymptomatic bacteruria
- Children with voiding dysfunction

## **3. Results**

The UTI prevalence rate in our study is 153/3050 (5.09% ). UTI distribution regarding gender is 112/153 (73.2%) females and 41/153 (26.8%) males. Patients were categorized as 1<sup>st</sup> febrile episodes in 106/153 cases (69.7%) distributed as 34 males and78 females while recurrent not initially investigated episodes in 47/153 cases (30.7%) distributed as 13 males and34 females.

Table 1: Distribution of UTI cases regarding gender and type of episode

Sex	Initial episode	Recurrent episode	Total	
Females	78	34	112	73.2%
Males	34	13	41	26.8%
Total	106	47	153	
	69.7%	30.7%		100%

The distribution of UTI cases in relation to age groups versus attack shows that: children less than 1 year old counted in 90/153 cases (58.8%), initial attack in 64 and recurrent episode in 26 patients. UTI in children between 1-2 years old registered in 26/153 (17%), initial episode in 17 cases and recurrent episodes in 9 cases. UTI in children between 2-5 years registered in 17/153 (11%) distributed as 9 initial episodes and 8 recurrent episodes. UTI detected in children aged more than 5 years counted in 20/153 (13%), initial episodes in 16 and recurrent episodes in 4 cases. To summarize, 116 /153 cases i.e 75.8% of all our patients are less than 2 years old. Another small rise in incidence is noted in children more than 5 years old.

Table 2: The distribution of our cases in relation to age groups versus attack.

Attack	< 1 year	12- 24 months	24-60 months	>60 months	Total
Initial	64	17	9	16	106
Recurrent	26	9	8	4	47
Total	90	26	17	20	153
	58.8%	17%	11%	13%	100%

The predominant etiological organisms are E. coli in 88.9% of cases. Proteus detected in 8.5% mostly in boys less than one year old and Klebsiella in 2.6%.

Table 3: The predominant etiologic organisms of infection.

E. coli	88.9%
Proteus	8.5%
Klebsiella	2.6%

Regarding clinical presentation, extra renal symptoms are predominant in 137/153(89.5%) children who are mainly aged less than 2 years. Renal symptoms are presented in 45/153 (29.4%), while combined renal and extra renal manifestations are presented in 29/153 (18.9%). The predominant renal symptoms include Dysuria in 21%, bedwetting in 9.2%, frequency in 8.5%, dribbling in 6.2% and bad smell of urine in 4%. On the other hand, the predominant extra renal symptoms include fever in 89%, diarrhea in 52.9%, vomiting in 48.4%, failure to thrive in 23%, dehydration in 17%, diaper dermatitis in 11% and cough in 9%.

Table 4: Type of clinical presentation

Clinical	Females	Males	Total
Urinary	36	9	45
Extra renal	100	37	137

Table 5: The predominant renal and extra renal symptoms

Renal		Extra renal	
Dysuria	21%	Fever	89%
Frequency	8.5%	Diarrhea	52.9%
Bed wetting	9.2%	Vomiting	48.4%
Dribbling	6.2%	Failure to thrive	23%
Bad smell urine	4%	Dehydration	17%
		Diaper dermatitis	11%
		Cough	9%

Risk factors found in our patients are: age less than 2 years in 75.8%, bad hygiene in 11.8%, uncircumcised boys in 7.8%, constipation in 5.9%, pinworm infestation in 5.2%, vulvovaginitis in 3.5%, renal stones in 3 cases 2% and labial fusion in 2 cases 1.3% (table 6).

Table 6: Risk factors.

Constipation	9 cases (5.9%)
Age < 2 years	116 cases (75.8%)
Uncircumcised boys	12 cases (7.8%)
Bad hygiene	18 cases (11.8%)
Vulvovaginitis	5 cases (3.2%)
Pinworms	8 cases (5.2%)
Labial adhesions	2 cases (1.3%)
Renal stones	3 cases (2%)

### 3.1 Ways to collect urine samples

Regarding our series, catheter urine samples are performed in 68 patients (44.5%), suprapubic in 46 cases (30%) while clean mid stream voiding sampling in 39 cases (25.5%).

### 3.2 Investigation of patients

The AAP guidelines 1999 were followed to investigate patients with febrile UTI by performing routine U/S of kidney and bladder during the 1<sup>st</sup> few days of treatment and VCUG at the end of treatment or within 2 weeks of diagnosis. DMSA scintigraphy was done on few selected patients to study renal function and parenchymal scarring. The aim of performing U/S and VCUG was to visualize the upper and lower urinary systems in both the febrile initial and recurrent episodes.

103 patients are subjected to imaging, 50 patients are missed either due to refusal of parents or have performed partial investigation (U/S only). The 103 cases who undergone imaging were distributed as 72 females and 31 males and revealed a total of 47/103 renal anomalies (45.7% of investigated cases). 31 males are investigated revealing 21 renal anomalies while the 72 females revealing 26 anomalies (table 8). The investigated patients were distributed as 65 cases presenting in their initial episode (21 males and 44 females) while recurrent not initially investigated episodes are 38 (10 males and 28 females). Initial episodes in both males and females turned to show 25 renal anomalies and recurrent episodes showed 22 renal anomalies. A total of 47 (45.7%) anomalies are detected including 25 cases of VUR (12 in male and 13 in females) are found in both initial and recurrent attacks (table 9, 10).

Table 9: Renal anomalies and VUR in males

Attack	Investigated males	Renal anomalies		VUR	
Initial	21	12		7/12	
Recurrent	10	9		5/9	
Total	31	21/31	67.7%	12	38.7%

Table 10: Renal anomalies and VUR in females

Attack	Investigated females	Renal anomalies		VUR	
Initial	44	13		5/13	
Recurrent	28	13		8/13	
Total	72	26/72	36%	13	50%

The 47 renal anomalies are located in upper and lower renal systems, detected in either initial or recurrent episodes presenting 67.7% of investigated males and in 36% of investigated females.

VUR is detected in 25 cases out of 47 total renal anomalies i.e.>50% distributed as follows:

- Grade I-II : 9 cases
- Grade III : 6 cases
- Grade IV : 6 cases
- Grade V: 4cases 3 of them needed surgery.

The renal anomalies are listed in table 11.

Table 11: List of renal anomalies

Anomalies	Number
Bilateral VUR	19
Unilateral VUR	6
Urethrovesical junction stenosis	3
Urethral stenosis	4
Right kidney with double ureters (absent left kidney)	1
Right mega ureter with no reflux	1
Left ectopic ureterocele	1
Left kidney with bifid ureter	1
Meatal stenosis	2
Left kidney with 2 ureters and one pelvis	1
Localized stenosis of the middle portion of right ureter	1
Labial fusion	1
Bladder diverticulæ	2
Two kidneys on right side	1
Hypertrophy of vermonatum	1
Posterior urethral valve stenosis	2

In addition to the 47 renal anomalies detected by U/S and VCUG, two cases of renal stones in the upper renal system and another two stones in the lower renal system are also detected. Regarding the yield of U/S and VCUG: U/S of kidneys and bladder could detect 17 renal anomalies (5 in males and 12 in females). VCUG could detect 30 more anomalies: 16 in males and 14 in females (table 12).

Table 12: Results of U/S and VCUG

	Males	Females
U/S	5	12
VCUG	16	14
Total	21	26

Considering that VUR grades IV and V are only serious anomalies, then corrected total renal anomalies are 32 out of 103 investigated cases (31%).

The leukocyte esterase and nitrite dipsticks in urine samples were not available in our hospital, so we performed microscopic urine analysis to evaluate pyuria and bacteruria. Bacteruria is evident in 65 cases (43.5%) while pyuria >10 WBC/HPF was evident in 40 cases (26 %).

#### 4. Discussion

**4.1.** The prevalence rate in our series is 5.09% which is close to the universal rate reported by AAP guidelines 1999 (7). This rate does not reflect the prevalence rate of Lebanon, since the study done on a limited number of patients, and over a localized suburban hospital.

**4.2.** The age of our patients ranged between 1 month and 12 years and presenting either in their first febrile UTI or in recurrent episodes, provided that their initial episode was not investigated. 75.8% of our UTI cases found to be less than 2 years old. It is reported that children less than 2 years are more prone to renal parenchymal damage as a consequence to febrile UTI (2). Female patients are predominant in our series, since 73.2% girls presented with febrile UTI. This coincides with the claim that girls are generally at increased risk of UTI especially if their age is less than 1-2 years (3)( 13).

**4.3.** Initial episodes of febrile UTI is registered in 106/153 cases while recurrent episodes registered in 41/153 cases. Both types revealed 47 renal anomalies: 25 renal anomalies in initial attacks and 22 renal anomalies in recurrent attacks (tables 9 and 10). This means that initial episodes as well as recurrent episodes are associated with risky renal consequences and need to be investigated (14).

**4.4.** The predominant etiologic organism detected by urine culture is E.COLI in 88.9% of cases which more or less coincides with what Brett White reported in 85% of UTI cases (1).

**4.5.** Regarding clinical presentation, extra renal symptoms and signs as fever, diarrhea or vomiting are more evident in children less than 2 years old, while older children manifest specific renal manifestations as Dysuria, bedwetting etc... (tables 4 and 5). So, in our series, clinical presentation found to depend on the age of the child meaning that age is directly related to renal symptoms and inversely related to extra renal symptoms. It is reported that children with upper respiratory or gastrointestinal symptoms and are not on antibiotics and not



immune compromised are considered as potential candidates of UTI. So, respiratory or gastrointestinal infections do not rule out febrile UTI (13).

**4.6.** The most predominant way to collect urine samples in our series is by catheter 44.5% and by suprapubic in 30% since most of our patients aged less than 2 years. So, the way to collect urine depends on the age of the patient and on the period of toilet training as AAP guidelines report (7).

**4.7.** Regarding investigating febrile UTIs, we followed the routine procedure advocated by the AAP guidelines 1999, since the patients of this study were evaluated in the years 2007 and 2009 before the great shift of AAP guidelines in 2011. 103 patients are investigated by doing U/S of kidneys and bladder in the first few days of febrile UTI and then doing VCUG at the end of treatment irrespective of the result of U/S aiming to visualize upper and lower renal systems including VUR(7) (12) (14). Both initial and recurrent episodes are investigated: In initial episodes, a total of 25 renal anomalies and another 22 anomalies detected in recurrent attacks. The 31 investigated males revealed 21 renal anomalies and the 72 investigated females revealed 26 anomalies (table 8). The 21 males in their initial episodes showed 12 renal anomalies out of which 7 cases of VUR while 10 males in their recurrent episodes revealed 9 renal anomalies including 5 cases of VUR. On the other hand, 44 females presented in their initial episodes showed 13 renal anomalies out of which 5 VUR cases were detected. In 28 females presenting with recurrent attacks, 13 renal anomalies out of which 8 VUR cases were detected. Out of these findings, we came with an opinion that both initial and recurrent episodes are worthy to be investigated. In our series, we found that U/S of kidneys and bladder could detect 17 renal anomalies and VCUG could detect another 30 renal anomalies which we considered a significant finding. Urine analysis microscopy is performed in our patients since dipsticks tests for leukocyte esterase and nitrite tests were not available in our hospital. Bacteruria was detected in 65 cases (42.4%), while pyuria more than 10 wbc/HPF found in 40 cases (26%). We found pyuria in our series helpful in a low number of cases; however, AAP guidelines 2011 stressed the role of urine analysis either by dipsticks or microscopy. They claimed that pyuria is important to support UTI but its absence does not rule out UTI (9). Alan S Peterson, also reviewed AAP guidelines 2011 and claimed in his revision that action statement 3 states that pyuria may be present in many conditions as Strep infection, Kawasaki and other conditions different from UTI. So, presence of pyuria does not confirm UTI and its absence do not rule out UTI (15).

## **5. Conclusions**

**5.1.** The prevalence rate of febrile UTI in our series is 5.09% involving children aged 1 month to 12 years. This does not reflect the real incidence in Lebanon, being studied in a sub urban region and covering a limited number of patients. Distribution regarding sex is 41 males (26.8%) and 112 females (73%). Distribution regarding type of UTI, initial episode in 116 patients and recurrent episode in 47 patients.

**5.2.** Performing an U/S of kidneys and bladder then a subsequent VCUG irrespective of U/S result showed a high significance, since it detected 47 associated renal anomalies out of total cases (app. one third of our febrile UTI cases) and 45.6% of our investigated cases 47/103 cases. So, the association of UTI with renal anomalies is high.

**5.3.** The yield of U/S is the detection of 17 renal anomalies. VCUG could detect 30 more renal anomalies. Thus, out of our series the role of both U/S and VCUG is important in the management of febrile UTI.

**5.4.** Initial episodes of UTI found to be associated with 25 renal anomalies while recurrent episodes showed 22 renal anomalies so both types of episodes must be investigated in both males and females.

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