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Research Paper

Clinical Prediction Criteria to Identify Febrile Young Children (0-5 Yrs) For Urinary Tract Infection

Medical Science

KEYWORDS : UTI, evaluation of febrile infants, prevalence

R. Arora VMMC& Safdarjung Hospital.New Delhi-110029

S.Bhanja VMMC& Safdarjung Hospital. New Delhi-110029

ABSTRACT

The study is thereby undertaken to formulate a clinical prediction criteria to identify febrile young children (<5yrs) at risk of UTI .It is a prospective study. Two hundred children younger than 5 years of age presenting to the ED with a fever (38.5°C) for more than 2 days who did not have a definite source for their fever and who were not on antibiotics or immunosuppressed. Otitis media, gastroenteritis, and upper respiratory infection were considered potential but not definite sources of fever. According to our study mean age of presentation is 2.6 years, most of culture positive group are females (73%).Significant number of patients with urinary tract infection had vomiting (31%), abdominal pain(55%), suprapubic tenderness(47%), irritability(50%), decreased oral acceptance (80%). Most common organism isolated in culture is E.Coli (69%). An effort was made for formulation of prediction criteria for less than 2 years and more than 2 years. Six criteria were included – female sex, fever more than 102 F, vomiting, irritability, decreased oral acceptance and abdominal pain to make the prediction model for culture positivity in febrile patients. .Presence of two or more criteria further increases the chance of having positive result. Sensitivity and positive predictive value of culture increased when 2 criteria are taken as compared when only one criteria is taken.

INTRODUCTION

Urinary Tract Infection (UTI), encompasses a spectrum of clinical and pathological conditions involving the various parts of urinary tract[1] .There are three forms of UTI: pyelonephritis, cystitis and asymptomatic bacteriuria. Differentiating the syndromes associated with urinary tract infection has important implication in treatment and prognosis of UTI.[1] | **It is one of the most commonly diagnosed infections of childhood**.[2] Prevalence of UTI, in febrile young children presenting to emergency department is 3-5%, in some studies it has been found to be as high as 30%.[3] The prevalence of UTI varies with age, sex, race, severity and duration of fever. [4,5,6] Urine culture is usually positive in 21% of the patients from whom culture is obtained.[8] Mean age of presentation of UTI is 7.6 yrs[9]. In 1st year of life male:female ratio is 2.8 to 5.4:1.In children more than 1yr of age ratio is 1:10.[10] After the first UTI, 60-80% of girls develop a second UTI within 18 months. Girls also have multiple infections [11]. However in boys peak age of UTI is first year of life, more common in uncircumcised male children[7] .Main causative organisms being Escherichia Coli which represents 70-80% of all cases of UTI, followed by Klebsiella pneumonae (3-6%) and proteus sp(3-6%)[1,6,7,3] . Majority of UTI occur by ascending route of infection. Majority of febrile children have pyelonephritis putting them at risk for renal scarring and possible long term sequelae of hypertension and renal failure. [13,14] Therefore it is important that physician identifies these children to institute early treatment and provide proper follow up. Symptomatology of UTI is highly variable with relation to the age of patient, sex of patient .Symptoms are usually hard to pinpoint. Infants usually presents with irritability,[15] vomiting, inability to feed, fever which comes out of nowhere and other non-specific symptoms. Young children may present with urinary symptoms namely frequency, urgency dysuria, low backache, abdominal pain, change in colour / odour / smell and blood in urine. It has been found that the most common symptom is fever and urinary tract symptoms.[8] Urine culture is considered the gold standard for the diagnosis of UTI.[4] A positive urine culture is defined as a growth of urinary tract pathogen $\geq 10^5$ CFU/ml[16] or 10^4 CFU/ml in a symptomatic patient. Pyuria in smear suggests infection but infection can occur in the absence of pyuria. This finding is more confirmatory than diagnostic[17,18.]

Often all children presenting to emergency and OPD with fever and nonspecific symptoms undergo a urine culture test routinely putting an unnecessary burden on hospital sources. No clinical criteria are yet followed so as to screen a child with febrile illness, who is at risk of having UTI. The study is thereby undertaken to formulate a clinical prediction criteria to identify febrile young children (<5yrs) at risk of UTI . Studies have been done previously attempting to correlate UTI with clinical finding such as fever, vomiting, diarrhea, poor feeding. However the results have been inconsistent.[19,20].

This study is an effort to identify specific clinical factors predictive of a positive urine culture and to use those factors to distinguish patient at low risk of UTI from those who need further evaluation.

MATERIAL AND METHODS

This study is carried out in the Department of Pediatrics, Safdarjung Hospital, New Delhi over a period of 1 year. This study is a prospective study. Study Group comprises of 100 patients fulfilling the inclusion criteria and Control Group constitutes 100 subjects coming with fever where urine culture is sterile.

Subjects of study include children ≤ 5 yrs of age having one or more of the following symptoms and signs

Fever duration ≥ 2days.

Temperature >38.30C

Children with urinary symptoms e.g. urgency, frequency, burning micturation, secondary incontinence.

Irritability decreased oral acceptance, vomiting, ill-looking child.

Previous history of UTI.

Urine routine microscopy positive for pus cells.

Children with nonspecific symptoms of Upper Respiratory Tract Infection, Gastroenteritis and Otitis Media.

Exclusion Criteria:

Children with definitive source of fever e.g. pneumonia, meningitis, cellulites, pharyngitis etc.

Children with urinary catheter in situ.

Children who have taken a course of antibiotic during the current episode of illness.

Complete clinical history and physical examination was performed. History specific for UTI and other systemic illness were

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taken to rule out illnesses pertaining to other system e.g. respiratory, gastrointestinal. A proforma was then completed. All children under inclusion criteria had undergone routine urine microscopy and urine culture examinations before initiation of antibiotic therapy. In toilet trained children, early morning midstream urine sample was taken. Parents were explained the method of urine collection. First urine containing most of the contaminating bacteria in the periurethral area is omitted. Urine collected under all aseptic precautions. In infants urine was collected by the application of a clean, adhesive sealed sterile collection bag. First skin was dried thoroughly after cleaning the periurethral area, child kept in the upright position to prevent urine coming in contact with skin or entering the vagina in females, the bag is voided immediately after the child has voided. For neonates catheterization was done with a no. 5 infant feeding tube and subsequently urine collected. Same sample for urine routine microscopy and culture was taken to avoid any discrepancy of results. Sample was cultured within 1-2 hr[s] of collection to avoid over growth which gives false positive results. If not feasible, samples for culture were stored in refrigerator (4-8^{0}C) for a maximum of 18 hrs.Smears are prepared using 2 drops of uncentrifuged urine on a slide within a standardized marked area (1.5 cm in diameter), air dried, fixed and gram stained. Average number of bacteria per oil immersion field was counted and their morphology recorded. Pyuria in smear suggests infection but infection can occur in the absence of pyuria. This finding is presumptive than diagnostic.

URINE CULTURE

Urine received in sterile container were inoculated onto sheep blood agar and Mac Conkey, plated with 3mm wireloop which delivers .01ml of urine, incubated at 35^0 C overnight. If there is no growth then it is again incubated upto 48 hrs. The sample is considered sterile in case of no growth. The antibiogram was done by Kirby-Bauer's method on Huller Hinton agar.

RESULTS

The mean age of presentation was found to be 2.6 years within a range of 1.5 months to 5.00 years for the proven urinary tract infection patients.Maximum number of patients was in 2-5 years age group. Majority [73%] of patients in the culture positive group were female. There was statistically significant difference with **p < 0.001** in two groups. UTI patients presented with wide range of temperature with a minimum of 101 F and maximum of 105 F and a Mean of 102.3 F.

It was observed that majority of patients with urinary tract infection had vomiting [63%], abdominal pain[55%], suprapubic tenderness [47%], irritability [50%], decreased oral acceptance [80%]. The results of all these symptoms when compared with their control group were statistically significant with a highly significant p value of less than 0.001

Some uncommon symptoms were dysuria [18%], pyuria [9%], hematuria [4%] and incontinence [1%].Majority of patients with UTI had fever duration more than 5 days at presentation. Patients with fever duration with more than 2 days were enrolled in the study group. The Study Group was than divided in two subgroups. Patients presenting within 5 days of illness were placed in one sub group, while other sub group included patients presenting after 5 days of illness.

Pus cellsinUTI patients varied from clear microscopy to 50 cells/mm^3 .In controls pyuria range from 0 -10 Cells per mm^3. Urine microscopy is positive in 44% of cases and 16% of controls with a significant p value of less than 0.000.

Therefore urine microscopy has a high positive predictive value of 73.3% and negative predictive value of 60%, odds ratio being 4.12. Thereby positive microscopy signifies 4.1 times more risk of having UTI than having no infection.Most common organism isolated is E.Coli (69%) followed by Klebsiella (17%),Enterococci (5%) Staphylococcus (3%). Symptomatology profile of patients less than 2 years and more than 2 years show marked difference as bladder control is usually achieved around this age. The 100 UTI patients were divided in two groups; One group constituted patients less than or equal to 2 years and second group 2 to 5 years. Symptoms are compared in the two groups.

Table 1:
Symptom comparison in two groups

	Age Group 2 Yrs and Below				Age Group Above 2 Years			
	Culture Positive [47 cases]		Culture Neg. [38 cases]		Culture Positive [53 cases]		Culture Neg. [62 cases]	
Abdominal Pain	21	(44.6)	0	(0)	34	(64.15)	20	(32.2)
Suprapubic Tenderness	23	(48.9)	0	(0)	24	(45.2)	16	(25.8)
GI Symptoms	20	(42.5)	24	(63.15)	17	(32)	20	(32.2)
Incontinence	1	(2.12)	0	(0)	0	(0)	4	(6.4)
Irritability	31	(65.9)	20	(52.6)	19	(35.8)	4	(6.4)

***figure in bracket implies percentage**

It was observed that supra pubic tenderness is comparable in two groups. However, incidence of abdominal pain is higher in more than 2 year age group. Irritability is more common in younger infants. An effort was made for formulation of prediction criteria for less than 2 years and more than 2 years.

Table no. 2: Univariate analysis of the significant predictors

	Predictor	P Value	Sensti-Vity	Speci-Ficity	Positive Predictiv Value	Negative Predictive Value	Odds Ratio Relative Risk [95% confidence Interval]
1	Sex [Females]	0.012	73%	44%	56.6	62.0	2.12 [1.17-3.84]
2	Fever > 102F	0.001	71%	52%	59.0	64.2	4.03 [2.2-7.8]
3	Vomiting	<0.001	69%	92%	89.6	74.8	25.59 [11-59.1]
4	Irritability	<0.001	50%	76%	67.6	60.3	3.13 [1.7-5.79]
5	Dec. Oral Aceptance	<0.001	80%	60%	66.7	75.0	6.00 [3.18-11.2]
6	Abdominal Pain	<0.001	55%	80%	74.6	61.3	4.89 [2.6-9.2]
7	Suprapubic Tenderness	<0.001	47%	84%	73.3	64.0	4.65 [2.39-9.03]
8	Pyuria on Microscopy	<0.001	44%	84%	73.3	60.1	4.12 [2.12-8.01]
9	Duration > 5 days	<0.001	56%	76%	70.0	63.3	4.03 [2.2-7.8]

All the above parameters are statistically significant with a significant

P value.(Table 2). Univariate analysis depicts that if one risk factor is considered the risk of having culture positivity has a sensitivity of 70-80% and a positive predictive value 60-70%.

After a detailed analysis of the data, six criteria were included – female sex, fever more than 102 F, vomiting, irritability, decreased oral acceptance and abdominal pain to make the prediction model for culture positivity in febrile patients. Positive predictive value and negative predictive value were then calculated taking each of these variables in different combinations.

Table no.3

Prediction Factors	Positive Predictive Value	Negative Predictive Value	P Value	Odds Ratio	Sensitii Vity %	Specificity %
Fever/ Irritability	81.8	59.0	<0.001	6.47 [2.8 -14.8]	36	92
Vomiting/ Dec. Oral Acceptance	93.5	69.6	<0.001	33.1 [11.3 – 97]	58	96
Vomiting/ Abdominal Pain	100	66	<0.001	-	49	100
Vomiting/ Irritability	88.6	58.2	<0.001	10.78 [3.6 – 16.8]	31	96
Dec. Oral Acceptance / Abdominal pain	83	60.1	<0.001	7.35 [3.2-16.8]	39	92
Dec. Oral Acceptance / Irritability	69.7	59.7	<0.001	3.4 [1.6 – 6.4]	46	80
Irritability / Abdominal Pain	100	54.7	<0.001	-	68	100
Female Sex / Vomiting	100	66.2	<0.001	-	49	100
Female Sex / Fever	69.6	62.8	<0.001	3.87 [2.1 – 7.1]	55	76
Female Sex / Dec Oral Acceptance	68.8	61.8	<0.001	3.57 [1.9 – 6.57]	53	76
Female Sex / Abdominal Pain	78.6	61.1	<0.001	5.7 [2.8 – 11.8]	44	88
Female Sex / Irritability	70.7	55.3	<0.001	2.99 [1.4 – 6.3]	29	88
Fever / Vomiting	93	67.1	<0.001	27.1 [9.2 – 79.3]	53	96
Fever / Dec. Oral Acceptance	77.8	65	<0.001	6.7 [3.4-12.99]	56	84
Fever / Abdominal Pain	84	61.3	<0.001	8.3 [3.6-19]	42	92

The above table shows that positive predictive value and negative predictive value is more in combination of criteria than on individual criteria basis. Also the sensitivity and specificity increases

Thus of the six criteria:Female Sex,Fever more than 102 F,Vomiting,Irritability,Abdominal Pain: and Decreased Oral Acceptance

Any one of these criteria present in a febrile child presenting to the emergency department, the risk of having urinary tract infection is high .Presence of two or more criteria further increases the chance of having positive result. Sensitivity and positive predictive value of culture increased when 2 criteria are taken as compared when only one criterion is taken .

DISCUSSION

Very few studies have been done to study the clinical profile of children urinary tract infection [20,15,] .These studies were done in different populations groups. Relevant data could not be found in Indian context. The purpose of this study was to analyze the clinical presentation of UTI in infants and children presenting at out patient department, with an idea to expedite diagnosis and thus reduce the morbidity associated with it.The mean age of patients in our study is 2.6 years. Male: female ratio in the first year of life is 1.4:1 and after one year 1: 4.7. This is in concordance with **Consensus statement on management of UTI by IAP Nephrology Group** [10] which documents male predominance in first year of life and female predominance thereafter. Female predominance was also seen in other studies[8] . **Quereshi et al** [20] designated fever to be most important parameter for UTI having significant diagnostic implication.In our study 63% of patients presented with 'vomiting'. In patients less than 2 years, 65% of patients had vomiting and between 2-5 years 60.3% had vomiting. The results are comparable in the 2 groups. **Quereshi et al** [20] reported dysuria to be common presentation in older children (4% to 60.8%). Similar finding were found in **Lizama et al** [8].In our study dysuria is reported in 18% of patients. . The difference seen in various studies is due to the difference in the patients age groups.Significant numbers [64%] of children more than two years with UTI reported abdominal pain .Suprapubic tenderness is noticed in 47% of cases. **Smellie et al** [15] reported abdominal pain in 23% patients between 2-5 years. Gastro Intestinal symptoms including diarrhea are reported in few patientsNo Indian data in however available in this regard. 65% of patients less than 2 years and 35% between 2-5 years complained of irritability. These non specific symptoms are mentioned as a significant factor for diagnosis in various studies but reliable data is not available. **Smellie JM et al** [15] reported 7% in less than two years and 9% between 2 to 5 years. AAP[4] also mentions that there is more risk of UTI if there is high degree of toxicity, dehydration and decreased oral acceptance.

Urine microscopy is the most important screening test for the initial analysis of UTI [4,]. 44% of our culture positive patients have evidence of pyuria in the urine routine analysis. Urine microscopy has a positive predictive value of 73% with a specificity of 84% and sensitivity of 44%. This result is statistically significant when compared with the control group. AAP[4]also recommends urine analysis screening test for selecting patients for prompt initiation of treatment while waiting for the results of urine culture.

Most common organism associated with UTI is found to be E. Coli. It is seen in 69% of patients. The results are comparable to most studies [8] . **Karyakarte et al** [12] documented changing etiology with klebsiella in maximum number of cases.

Our Study revealed a strong correlation between urine culture positivity in UTI patients and female sex, fever more than 102 F, decreased oral acceptance, vomiting, abdominal pain and irritability. These factors can be taken as prediction criteria; even if one is present the chances of having culture positivity are high with a sensitivity of 65-70% and positive predictive value of around 70%.If two parameters are present sensitivity increases to 80% and positive predictive value of 85%. Though the model has excellent sensitivity and specificity but further work is necessary to validate the results in different patient populations.

Although the prediction criteria will perform well in the population in which it has been derived, it has not been prospectively validated. Such validation is crucial because prediction rules generally fail to perform as well when subsequent

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