

THE ROLE OF QUANTITATIVE C-REACTIVE PROTEIN, WHITE BLOOD CELL COUNT AND PYURIA IN PREDICTING URINARY TRACT INFECTION AMONG FEBRILE INFANTS AND CHILDREN

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ABSTRACT

Introduction

Urinary tract infection (UTI) is among the commonest bacterial infections in infants and children that warrants early detection and management to prevent long term consequences in kidney causing significant morbidity. The prevalence of UTI varies according to age, gender, race, circumcision status of children but it occurs in 1% of boys and 1 to 3% of girls. There have been studies that have highlighted the importance of C-reactive as an inflammatory marker involved during urinary tract infection in children.

Objectives

To find out how Quantitative C-reactive protein level, white blood cell count and pus cells in urine are associated in febrile infants and children with UTI.

To find out the antibiotic sensitivity pattern of UTI.

Methodology

A prospective cross sectional study was conducted to evaluate febrile infants and children of 2 months to 13 years of age with suspected UTI for a period of six months. Venous blood samples were sent for Quantitative estimation of CRP, White blood cell count and urine samples were sent for urine microscopy and culture sensitivity. Statistical analysis of data was done using SPSS software version 16.

Results

Among 210 infants and children enrolled in the study, 62 (29.55%) had positive urine culture, representing 31.2% and 28.6% of female and male populations respectively.

The sensitivity, specificity, positive predictive value (PPV) and negative predictive (NPV) value of CRP (with cut off of 1mg/dl) was 77%, 81%, 63% & 90% respectively and that of WBC Count (with cut off of > 12000/ml) were 56%, 88%, 66% & 83% respectively. Similarly for pyuria (with cut off of > 10/HPF) using urine culture as gold standard were 63%, 91%, 74% and 85% respectively. The most common organism found in urine culture was E. coli 49(79%). Highest number of isolates were sensitive to Nitrofurantoin (96%) and Amikacin (94%) whereas Amoxicillin was resistant to all the organism tested that was the resistance of 100%. The next common antibiotics found to be resistant was cotrimoxazole (70%).

Conclusion

Quantitative C-reactive protein and White blood cell count in blood are very useful markers to predict UTI in febrile infants and children. E coli is the commonest pathogen to cause UTI and Pyuria (pus cells > 10/HPF) has high predictive value for UTI.

KEYWORDS

C-reactive protein, pyuria, urinary tract infection, white blood cell



INTRODUCTION

Urinary tract infection is one of the common bacterial infection in infants and children that warrants early detection and management to prevent long term consequences in kidney causing significant morbidity. Urinary tract infection not only involves bladder but the infection can ascend up to the kidney causing scarring of kidney that can cause hypertension and chronic kidney disease etc.^{1,2} The prevalence of UTI varies according to age, gender, race & circumcision status of children. but it occurs in 1% of boys and 1 to 3% of girls.³ There is male preponderance for UTI in less than 1 year age group whereas it is more common in female after infancy. One of the study done in Dhulikhel Hospital, Nepal reported UTI to be twice more common in female than male.⁴

There have been studies that highlighted the importance of C-reactive as an inflammatory marker involved during urinary tract infection in children and also underscoring the predicting value of raised WBC counts, ESR, mean platelet volume and lymphocyte -neutrophil ratio in detecting UTI early on.⁵⁻⁷ Different studies done to look at sensitivity and specificity of C-reactive protein, White blood cell count & pyuria have provided good evidence to support that they are useful in predicting UTI.⁸

The most common causative agents for UTI are fecal flora that colonizes around the perineal region and enters the bladder through urethra. Once infection commences, immune system gets activated leading to inflammatory response in the body.

Urine culture remains gold standard test for UTI but it takes 72 hours to isolate the organism and testing for sensitivity to the antibiotics that might delay treatment.⁹

Hence to predict the possibility of UTI very early on among febrile infants and children, we aimed to do this study to see whether quantitative estimation of CRP, WBC Count and pus cells in urine could predict UTI. We also aim to find out local sensitivity pattern for the common pathogens causing UTI.

METHODOLOGY

A prospective cross sectional hospital based study was conducted for a period of six months commencing from May 2017 to October 2017 at Biratnagar Asptal Pvt. Ltd. unit of Birat Medical College & Teaching Hospital, Biratnagar.

All the children (2 months-13 years) with fever (38.4°) and suspected to have urinary tract infection were included in this study. The symptoms included for the suspicion of UTI were vomiting, back pain, pain abdomen, foul smelly urine, urinary frequency & urgency etc. Those children also underwent history and physical examination. The children with diagnosed renal disorders & history of intake of antibiotics over the last one week period were excluded from the study.

Informed consents were taken from the parents and ethical approval was obtained from the research and ethics

committee of the hospital.

The blood was collected using BD Vacutainer from the peripheral vein using all aseptic precaution and serum was separated by centrifuging the vacutainer. The quantitative analysis of CRP was done on MISPA13 automated protein analyzer. Quantitative nephelometry method was used to quickly and accurately measure the specific level of CRP in serum. A smart card was inserted in the analyzer. A pre filled cartridge of CRP was taken and was tapped to remove any air bubble. Eighty microlitre of sample was added to the dedicated well in the cartridge and it was placed in the cartridge carrier. The start button is pressed and sample was analyzed. The test results were measured in mg/dl keeping a cut off of <0.6 mg/dl.

Appropriately collected urine sample was sent for microscopic examination of urine and culture sensitivity. The physical examination of urine was done to note the colour, odour, clarity and cloudiness. The chemical examination of urine was done by dipstick method using DEKA PHAN dipsticks from ERBA LACHEMA for protein, sugar, blood, specific gravity, pH, Ketones nitrites and leucocytes and urobilinogen.

Urine culture was considered gold standard test for UTI. For standard urine analysis pyuria was defined as >10 WBC count in centrifuged urine sample. Inoculation of urine was done using 0.01ml(x100) loop onto nutrient and Macconkey Agar. Loop full of urine was taken and streaked across the plate perpendicular to the original inoculum (Lawn Culture). Plates were inoculated at 37°C for 24-48 hours. Organisms were identified by doing naked eye examination (color) of the colonies and further by doing biochemical examination. The antibiotic sensitivity test was done on Muller- Hinton Agar.

All the data were entered in excel and transferred to SPSS version 16. The descriptive and inferential statistics were used for data analysis. The test of significance was done by chi square test. The sensitivity, specificity, negative predictive value and positive predictive value were calculated for CRP, WBC Count and Pyuria using Urine culture as the gold standard. A p value < 0.05 was considered significant.

RESULT

This study included 210 infants and children who met the inclusion criteria. Among them 30(14%) were from 2 months to <1 year age group, 113(53%) were in 1-4 years age group and 67(31%) were in >5 yrs - <12 years age group (Table 1). There were 133 (63%) male and 77 (37%) female in the study population out of which 38 (28.6%) male and 24 (31%) female had urine culture positive confirming urinary tract infection (Table 2). Similarly, out of 30 infants of 2 months to <1 year age group 12 (40%), out of 113 children of 1-5 years age group 35(31%) and in the >5 years age group



Table 1: Demographics of patients with positive culture results

Age group	Urine Culture	
	Positive	Negative
2 month to < 1 yr	12 (40%)	18 (60%)
1 yr to 4 yrs	35 (31%)	78 (69%)
5 yrs to <12 years	15 (22.4%)	52 (77.6%)

Table – 2: Culture Positivity in Different Sexes

Sex	Urine Culture		P Value
	Positive	Negative	
Female	38(28.6%)	95(71.4%)	0.7*
Male	24(31.2%)	53(68.8%)	

*Statistically not significant

15(29.5%) had positive urine culture.

The sensitivity, specificity, positive predictive value (PPV) and negative predictive (NPV) value of CRP with cut off of 1mg/dl, using Urine culture as gold standard were 77%, 81%, 63% and 90% respectively.

Similarly, the sensitivity, specificity, PPV and NPV of WBC counts in predicting positive urine culture were 56%, 87%, 66%, 82% respectively and for pyuria> 10/HPF the value were 61%, 90%,74% and 85% respectively (Table 3). Raised CRP of > 1mg/dL, Pus cells in urine >10/HPF and WBC count >12000/ml had high chances of having positive urine culture which was statistically significant (p Value < 0.001). The most common organism found in urine culture was E. coli 49(79%) followed by Staph aureus 5(8%), Klebsiella 3(5%), Pseudomonas 3(5%) and Proteus 2 (3%) as shown in (Figure-1). In this study the most sensitive antibiotics were Amikacin (96%) and Nitrofurantoin (96%) followed by Cefotaxime (95%), Cloxacilin (91%) and Cefixime (88%). It is interesting to note that all the organisms that were tested against Amoxycillin were resistant. The next common antibiotics found to be resistant was cotrimoxazole, in which 70% of tested organisms were resistant (Figure – 2)

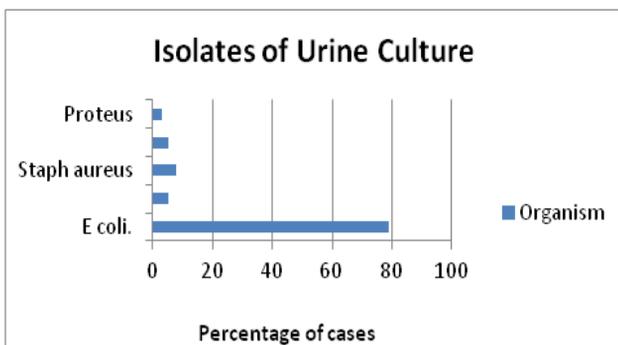


Figure 1 : Isolates of Urine Culture

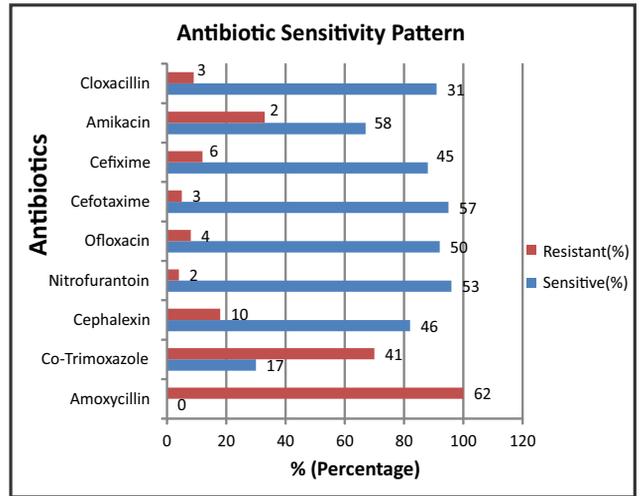


Figure 2: Antibiotic Sensitivity Pattern

Table 3: Sensitivity, Specificity, PPV, NPV of lab results

	Positive	Negative	Pvalue	Sensitivity (%)	Specificity(%)	PPV(%)	NPV(%)
CRP							
>1 mg/dL	48(63.2%)	28(36.8%)	<0.001*	77	81	63	90
<1 mg/dL	14(10.4%)	120(89.6)					
WBC							
>12000/ml	35(66%)	18(34%)	<0.001*	56	87	66	82
<12000/ml	27(17.2%)	130(82.8%)					
Pyuria							
>10/HPF in urine	39(73.6)	14(26.4%)	<0.001*	61	90	74	85
<10/HPF in urine	23(14.6)	134(85.4)					

*Statistically significant

DISCUSSION

Early diagnosis and treatment of UTI is of great importance due to its implication of renal scarring and its long term morbidity. Several studies done in various settings have clearly suggested that there is a raised inflammatory marker during urinary tract infection.^{1,2}

This study tried to look at the role of common inflammatory markers such as C-reactive protein and white blood cell count that we commonly use in our setting. In our study we found slightly higher prevalence of UTI (31%) among female children as compared to male children (28.6%).

Our study also noted that the prevalence of UTI is higher in infants (40%) as compared to children of 1-5 yrs age group (31%) or children of more than 5 yrs of age group (29.5%).

In our study we observed that the increased White blood cell counts of >12000/dl had sensitivity of 56.5% and specificity of 87.8% in predicting positive urine culture whereas the positive predictive value and negative predictive value were 66% and 83% respectively. However, Benador et al found a sensitivity of 89% and specificity of 25% in his study.¹⁰

In this study, we noted sensitivity and specificity of 77% and 81% respectively for CRP > 1 mg/dl taking Urine culture as the gold standard whereas PPV and NPV were 63% and 90% respectively which is different from the study done by Ayazi P et al in which the sensitivity was much higher(96%) and specificity was very low but Positive predictive value and NPV are comparable.¹¹ We also looked at the role of Pyuria



(pus cells > 10 /HPF) in predicting positive urine culture and noted that it has sensitivity of 62%, specificity of 90%, PPV of 74% and NPV of 85%. A study done by Al-Daghistani observed very high specificity (86.5%) for pyuria (Pus cells>10/HPF) which is close to our observation but the sensitivity was very low.¹²

The most common organism found in urine culture was *E. coli* 49(79%) followed by *Staphylococcus aureus* 5(8%), *Klebsiella* 3(5%), *Pseudomonas* 3(5%) and *Proteus* 2 (3%). A study done in Shiraz University of medical science also noted *E.coli* to be the commonest pathogen(51.5%) followed by *Klebsiella* (16.8%) and *Enterococcus sp* (9.9%).^{13,14} In our study, the most sensitive antibiotics were Amikacin (96%) and Nitrofurantoin(96%) followed by Cefotaxime (95%), Cloxacilin(91%) and Cefixime (88%). It is interesting to note that all the organisms that were tested against Amoxycillin were resistant. The next common antibiotics found to be resistant was cotrimoxazole, in which 70% of tested organisms were resistant (Figure - 2). A study was done in similar age group of children by Ojha et al and they also found resistance to cotrimoxazole (65%) which is consistent with our finding.¹⁵ In a study conducted at Bielanski Hospital Warsaw, high sensitivity of organisms like *E.coli* to second and third generation cephalosporins (80.5 - 90.3%), Amoxy clavulanic acid(71.7%) and even to Ampicilin (41.6%) was found. Although this finding was quite different from our study, it highlighted the importance knowing local antibiotic sensitivity pattern to provide

rational antibiotics prescription to treat infection.¹⁶ In a study done by Ojha A et al. in Nepal, Nitrofurantoin(93%) and Amikacin(93%) were the most sensitive which is comparable to our study. The finding from Gallegos J et al noted even higher percentage of sensitivity to Amikacin (100%) and Nitrofurantoin(100%).^{15,17}

CONCLUSION

Quantitative C- reactive protein and White blood cell count in blood can predict UTI in febrile infants and children with high sensitivity and specificity . Pyuria (pus cells>10/HPF) also has good sensitivity , positive and negative predictive value for predicting UTI. *E coli* being the commonest organism isolated. There is growing resistance of organism that warrants development of antibiotic guideline locally.

LIMITATION OF STUDY

This study was conducted for 6 months period only. Similar study for longer duration would have had better external validity.

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CONFLICT OF INTEREST

None

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