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A study of Quantitative Urinary C-Reactive Protein Level in Children with Urinary Tract Infection

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I. Introduction

Urinary tract infection (UTI) is a risk factor for kidney damage and end stage renal disease in children. It occurs in 3-5% of girls and 1% of boys and has three forms: acute pyelonephritis (APN), cystitis, and asymptomatic bacteriuria. Among them, APN, which may result in renal scarring in up to 64% of the patients, has more mortality and morbidity [1]. Early diagnosis and treatment of acute pyelonephritis is very important; otherwise, renal scar and other complications such as hypertension and renal damage may occur [2]. Clinical signs and symptoms and routine paraclinical findings in children cannot distinguish between upper (pyelonephritis) and lower UTI (cystitis)[3]. TC99m-Dimercaptosuccinic acid (DMSA) scan is the standard method to diagnose acute pyelonephritis [4-7]. This technique is invasive and expensive and is not available everywhere; therefore, investigation to find other diagnostic methods has been developed [8]. In a study by Anderson L, the quantitative level of urine proteins like C reactive protein (CRP), 1- alpha microglobulin and retinol binding protein (RBP) showed a significant relationship with pyelonephritis and renal damage using DMSA scan findings [9]. In this study, the urine level of CRP in the patients with UTI was higher than the patients with other febrile diseases [9]. CRP is an acute phase reactive protein which is measurable quantitatively [10,11] and can be produced in the kidneys locally [12]; therefore, a relationship is possible between urine CRP and renal damage in pyelonephritis. In this study, we compared the urine quantitative level of CRP in patients with UTI and patients who had other febrile infectious diseases; moreover, by performing DMSA scan in patients with UTI, were evaluated the role of CRP as a predictor of renal injury.

II. Material And Methods

This case control study was conducted between November 2014 and July 2015 after Institutional Review Board and Ethics Committee approval was obtained. Children with urinary tract infection who were hospitalized at HI TECH Medical college & Hospital of Bhubaneswar, India, were enrolled in the study as the case group after obtaining informed consent from their parents. The control group was chosen from patients with other bacterial infectious diseases except UTI. The diagnosis of UTI was based on the positive culture of a urine specimen defined as a voided urine specimen with isolation of a single bacterial strain in the quantitative count of $\geq$ 105 cfu/ml [13], more than 8 white blood cells (WBC) per high- power field (HPF) in the specimen and urinary signs and symptoms like fever, dysuria, frequency, weight loss, vomiting, and in children younger than two years, irritability and poor feeding. Children with genitourinary malformations or neurological diseases or acute diarrhea were excluded from the study. Urine specimens were obtained from all the patients within 24 hours after hospitalization and were stored at -60^{o}C. When sampling was finished, quantitative urine CRP was measured with the ELISA method using Hs-CRP kits (Diagnostic Biochem Canada Inc.®) in a laboratory. Demographic data like sex, age, weight and height were taken from the patients and laboratory findings like Na, K, Ca, Cr ,BUN, Plt , WBC, U/A , U/C were collected from their hospital files (Table 1, 2, 3, and 4). Children with UTI were referred to the nuclear medicine department for the DMSA scan and VCUG to detect parenchymal defects and vesicoureteral reflux (VUR). Children with normal absorption and renal function more than 45% in DMSA scan were enrolled in class 1, abnormal absorption and renal function more than 45% in class 2, and renal function between 40-44% and less than 40 % with abnormal absorption rate were in class 3 and 4, respectively [14]. Because of the abnormal distribution of the data, Mann-Whitney Test was used for analysis using SPSS software. P values less than 0.05 were considered statistically significant.

III. Results

We studied 50 UTI patients (42 girls, 8 boys) as the case group and 20 patients with other infectious diseases (8 girls, 12 boys) as the control group (Table 1, 2). The mean ±SD age of the cases and controls was 36.7 ±31.57 and 40.37± 40 months respectively, ranging from 2 months to 12 years old (Table 1, 2). Demographic data of study group are shown in tables 3 and 4. The mean ±SD urine CRP was 224.8±320.1 in

patients with UTI and 179.76±182.6 mg/L in the control group (Table 5). There was no significant difference between groups (P value 0.83). The mean ±SD urinary CRP was 83.4 ± 46.02 mg/L in 9 patients with DMSA scan class 1, 224.8±320.1 mg/L in 38 patients with class 2, and 399.53 ± 46.27 mg/L in three patients with class 3 (Table 7). The mean urine CRP had no statistically significant difference between patients with different classes of DMSA scan (Table 6, 7). A total of 4 patients had positive VCUG but there was no significant relationship between urine CRP and the results of VCUG.

Table 1: Demographic characteristics of the cases and controls

	Mean ±SD	P value
Age (months)		
Case	36.7±31.57	0.68
Control	40.35±40.14	
Height (cm)		
Case	83.1±26.35	0.34
Control	89.3±23.62	
Weight (kg)		
Case	13.8±7.41	0.96
Control	13.9±8.79	

Table 2. Urinalysis data of the groups (case dan control)

	Mean ±SD	P value
WBC		
Case	41.1±29.3	0.001
Control	2.0 ±1.16	
keton (positive)		
Case	83.1±26.35	0.34
Control	89.3±23.62	
RBC		
Case	3	o.56
Control		
Nitrit (positive)		
Case	2	0.005
Control	0	

Table 3. Blood count results of the groups (case and control)

	Mean ±SD	P value
WBC		
Case	20563±31619.61	0.54
Control	16015± 16515.04	
PLT		
Case	321794±1.32	0.51
Control	347825±1.87	
Hb		
Case	10.91±0.98	o. 6
Control	10.17±1.4	

Table 4. Serum electrolytes data of the groups (case and control)

	Mean ±SD	P value
Cr		
Case	0.±0.15	0.186
Control	0.5±0.11	
BUN		
Case	10.4±3.41	0.69
Control	10.1±4.17	
Na		
Case	139.3±2.78	0.43
Control	139.9±3.15	
K		
Case	4.51±1.0	0.7
Control	4.42±0.5	
Ca		
Case	10.09±0.62	0.7
Control	9.6±0.59	

Table 5. Mean urinary CRP in case and control groups

	N	Mean ±SD	P value
Urine CRP			
Case	50	244.8±320.1	0.186
control	25	179.6± 182.6	

Table 6. Relationship between urine CRP and DMSA scan results in the case group

DMSA SCAN	N	Mean ±SD	Mean Rank	P value
Urine CRP				
Normal	9	83.4±46.1	22.50	0.64
Abnormal	41	285.2±343.3	26.16	

Table 7. Relationship between urine CRP and DMSA scan classes 1, 2, 3

Urine CRP			
	N	Mean ±SD	P value
DMSA Scan			
Class1	9	83.4±46.02	
Class2	38	270.82±338.2	0.002
Class3	3	399.53±46.27	

IV. Discussion

Urinary tract infection (UTI) is a common problem in children and also a major cause of renal parenchymal injury. The standard method to detect these complications of UTI is the DMSA scan [4-7] but because of being invasive and expensive, substitute methods are being investigated [8]. One of these methods is measurement of the urinary or serum proteins and one of these proteins is CRP. Pecil et al evaluated serum CRP in children with UTI; they found that the sensitivity and specificity of serum CRP in detecting acute pyelonephritis was 96.4% and 31.9% respectively and reported a relationship between the severity of renal injury in DMSA scan and serum CRP although there no similar relationship was observed in the second DMSA scan after 6 months [15]. On the other hand, some studies have showed the low sensitivity and specificity of serum CRP in predicting renal injury or scar. Findings of studies by Naseri [16] and Turelinekx [17] indicated that serum CRP had a great diagnostic value in the diagnosis of UTI but it could not distinguish cystitis from pyelonephritis and also could not determine the severity of renal involvement. Anderson et all investigated the relationship of DMSA scan and urinary CRP in children with UTI and found that the mean level of urinary CRP in patients with UTI was higher than healthy individuals but there was no significant relationship between urine CRP and DMSA scan classes [9], although some studies suggest that the measurement of urinary CRP could be a tool to detect and evaluate possible kidney damage [15,18], our study showed no difference in the mean urinary level of CRP between patients with urinary tract infection and patients with other infectious diseases and no statistically significant relationship between urinary CRP and DMSA scan or VCUG results.

V. Conclusions

According to our study results, it seems that urine CRP is not a suitable predictor for renal injury or scarring caused by urinary tract infection and DMSA scan is the gold standard method for detecting the severity of renal involvement in UTI.

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