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Original Research Article

A Case-Control Study to Assess Procalcitonin Serum Levels in Children Under the Age of Five with UTI

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Abstract

Aim: The aim of the present study to evaluate the Procalcitonin Serum Levels in Children Younger than Five Years Old with Urinary Tract Infection. **Methods:** This case-control was done the Department of Paediatrics, Government Medical College, Bettiah, West Champaran, Bihar, India for 1 year. The 100 (100 case and 100 control) children less than 5 years of age were included in this study. The children in the case group suffered from UTI based on a positive urinary culture test. They also were undergone VCUG and accordingly were divided into two groups: having VUR and not having VUR. Their serum levels of PCT were measured before starting antibiotic therapy using the chemiluminiscence immunoassay (CLIA). They had negative results for both urine culture (UTI) and urinary analysis tests that the serum levels of PCT were measured for them. In both groups children under 5 years without genetically diseases and chronic kidney diseases included in the study. **Results:** Of the samples, 130 children (65%) were female. The median age of the samples was 23.7 months with an interquartile range between 11.5 and 36.5 months. Accordingly, both the evaluation methods diagnosed 90 children to be healthy, while 92% of children with VUR positive simultaneously were PCT positive. The odds of one positive and two positive for one way 1.714 (P=0.015) times and 1.212(P=0.785) times were higher than the group without reflux. However the odds of 4 positive for one way 0.239 (P=0.3) times was lower than control group. The positive and negative predictive values of the serum level of PCT were 40% and 90%, respectively. In this respect, 50% of the samples diagnosed by serum level of PCT were false positive and 12% were false negative. It meant that sensitivity and specificity of PCT measurement were 90% and 50%, respectively. The kappa score for the level of serum PCT was 0.5 (P < 0.0001). The positive predictive value of serum PCT for the female and male samples was 42% and 54% respectively. **Conclusion**: No statistically significant relationship between vesicoureteral reflux and the serum level of PCT.

Keywords: Procalcitonin, Children, UTI

Introduction

The most common cause of pediatric patients visiting the emergency room is fever.[1] Among them, especially those under 3 months, fever is often caused by a bacterial infection and it should be differentiated through examination.[2] According to some reports, the prevalence of severe bacterial infection (SBI) in infants under 3 months is only 10%, although in some developing countries, it is close to 30%, which places a heavy burden on the country.[3]

Procalcitonin is the precursor for calcitonin and is produced by parafollicular cells. It is a 116-amino acid protein that has roles in calcium metabolism.[4] PCT is elevated during infection and typically rises within two hours of the onset of a bacterial infection reaching a peak at 24 to 36 hours.[4] Procalcitonin levels are attenuated by the presence of interferon gamma that is typically released during viral infections leading to suggestions that PCT may have uses in distinguishing viral from bacterial infections.[4] The existing literature regarding the test accuracy of PCT in children is favourable with at least five meta-analyses demonstrating that PCT is accurate when used to diagnosis SBI across a range of paediatric settings.[5-9] The two most commonly used PCT cut-offs are 0.5 ng/ml and 2.0 ng/ml.[5-9] The lower cut-off of 0.5 ng/ml typically provides an approximate 80% sensitivity for the identification of SBI whereas the higher cut-off of 2.0 ng/ml typically provides a specificity of around 90%.[5-9] Two of the five meta-analyses compared PCT to CRP with both studies reporting that PCT was more accurate than CRP for the diagnosis of SBI in children.[8,9] PCT has also been shown to be particularly useful in the assessment of febrile young infants under 90 days of age.[10-12] As technology evolves, there is increasing interest in the use of point-of-care (POC) biomarkers for the early recognition of SBI. There have been a number of studies exploring the use of POC CRP testing to identify SBI at presentation to healthcare.[13,14] These studies have reported that the use of POC CRP can help to risk stratify children at triage/initial assessment.[13] Procalcitonin testing may however, represent the ideal POC test for detecting SBI in children due to its greater test accuracy.

Material and Methods

This case-control was done the Department of Paediatrics, Government Medical College, Bettiah, West Champaran, and Bihar, India for 1 year, after taking the approval of the protocol review committee and institutional ethics committee. The 200 (100 case and 100 control) children less than 5 years of age were included in this study. The children in the case group suffered from UTI based on a positive urinary culture test. They also were undergone VCUG and accordingly were divided into two groups: having VUR and not having VUR. Their serum levels of PCT were measured before starting antibiotic therapy using the chemiluminiscence immunoassay (CLIA). Those in the control group were UTI negative children that referred to the same healthcare setting for routine vaccination. They had negative results for both urine culture (UTI) and urinary analysis tests that the serum levels of PCT were measured for them. In both groups children under 5 years without genetically diseases and chronic kidney disease included in the study. Data collection tools were conducted based on a researcher-made questionnaire consisting of demographic questions, and questions regarding the laboratory and imaging results.

The data was analyzed via the SPSS software for windows. The descriptive and inferential statistics used in this study were percentage, independent t-test, Chi-squared test, and Roc curve.

Results

Of the samples, 130 children (65%) were female. The median age of the samples was 23.7 months with an interquartile range between 11.5 and 36.5 months. Although, 66% of them had no vesicoureteral reflux, 22% and 12% of the samples suffered from severe unilateral VUR and sever bilateral vesicoureteral reflux, respectively. The VCUG and the serum status of PCT were compared between the groups. Accordingly, both the evaluation methods diagnosed 90 children to be healthy, while 92% of children with VUR positive simultaneously were PCT positive. The odds of one positive and two positive for one way 1.714 (P=0.015) times and 1.212(P=0.785) times were higher than the group without reflux. However the odds of 4 positive for one way 0.239 (P=0.3) times was lower than control group. Considering the number of cases, we rely only on descriptive statistics for other groups. According to our findings, 62% of the samples were positive with regard to the level of serum PCT. One-half of those samples (62 people) who was diagnosed to be healthy using VCUG had a normal level of serum PCT. However, 38 people of the samples diagnosed to be healthy using voiding cystourethrogram had a positive result of level of serum PCT. The positive and negative predictive values of the serum level of PCT were 40% and 90%, respectively. In this respect, 50% of the samples diagnosed by serum level of PCT were false positive and 12% were false negative. It meant that sensitivity and specificity of PCT measurement were 90% and 50%, respectively. Globally, the odds of negative VUR were 10 times higher than positive VUR. In addition, the odds of negative VUR were 30 times and 3.12 times higher than positive VUR in males and females, respectively.The kappa score for the level of serum PCT was 0.5 (P < 0.0001) (Table 2). Accordingly, the sensitivity of the level of serum PCT for the female samples was 82% and for male samples were 100%. Additionally, the specificity of the serum PCT for the female and male samples was 38% and 62%, respectively. The positive predictive value of serum PCT for the female and male samples was 42% and 54% respectively (Table 3).

Table 1: The frequency of the diagnosis of VUR based on the evaluation method

Group	VCUG	Procalcitonin		Kappa	Odds ratio	P VALUE
		Control number (%)	Case number (%)			
Total	Control=100	58 (58)	42(42)	0.5	9.3	<0.0001
	Case=100	42 (42)	58 (58)			
Boy= 70	Control	44(22)	20 (10)	0.62	2.9	0.004
	Case	(0)	6(3)			
Girl= 130	Control	60(30)	20 (10)	0.177	3.03	0.032
	Case	10 (20)	40 (20)			

Table 2: The frequency of the diagnosis of VUR based on gender

Symmetric measures Gender		Value	Asymp. std. error[a]		Approx. T[b]	Approx. sig.
Girl	Measure of Agreement	Kappa	.191	.063	2.52	.027
	N of Valid Cases		150			
Boy	Measure of Agreement	Kappa	.545	.142	2.39	.003
	N of Valid Cases		50			
Total	Measure of Agreement	Kappa	.361	.078	3.12	.002
	N of Valid Cases		200			

Table 3: The frequency of the diagnosis of VUR based on the evaluation method and gender

VCUG * Procalcitonin* gender Cross tabulation

Gender				Procalcitonin Ill		Total Healthy
Female	**VCUG**	**Healthy** Count % within VCUG		34a 34%	66b 66%	100 100%
		% within Procalcitonin		78%	60%	66%
		Ill	Count	12a	38b	50
			% within VCUG	24%	76%	100%
			% within Procalcitonin	20%	60%	40%
	Total		Count	25	55	80
			% within VCUG	31.25%	68.75%	100.0%
			% within Procalcitonin	100%	100%	100%
Male	**VCUG**	**Healthy**	Count	15a	5b	20
			% within VCUG	75%	25%	100%
			% within Procalcitonin	100%	50%	76%
		Ill	Count	0a	8b	8
			% within VCUG	0.0%	100%	100%
			% within Procalcitonin	0.0%	50%	24%
	Total		Count	12	8	20
			% within VCUG	60%	40%	100%
			% within Procalcitonin	100%	100%	100%
Total	**VCUG**	**Healthy**	Count	38a	42b	80
			% within VCUG	47.5%	52.5%	100.0%
			% within Procalcitonin	92%	53%	80%
		ill	Count	3a	17b	20
			% within VCUG	15%	85%	100.0%
			% within Procalcitonin	15%	45%	35%
	Total		Count	40	60	100
			% within VCUG	40%	60%	100%
			% within Procalcitonin	100 %	100%	100%

Discussion

Serious bacterial infections are often difficult to differentiate from viral infections during the prodrome. It has been suggested that PCT may be superior to CRP for the diagnosis of SBIs in children. The measurement of serum level of PCT as a biomarker using a non-invasive method is recognized for an early detection of UTI and VUR.[15-24] PCT has been demonstrated to be correlated to both acute pyelonephritis and late renal scars and predict VUR in children with UTI. [17] In our study, 130 children (65%) were female. The median age of the samples was 23.7 months with an interquartile range between 11.5 and 36.5 months. Although, 66% of them had no vesicoureteral reflux, 22% and 12% of the samples suffered from severe unilateral VUR and sever bilateral vesicoureteral reflux, respectively. In other two studies, VUR was found in 26% and 11% of children respectively.[19] The serum level of PCT more than 0.5 ng / ml is considered abnormal and may indicate sepsis.[15] Daily measurements of PCT can determine the adequacy and duration of antibiotic therapy as well as the patient's prognosis. This is specifically important in the early stages of sepsis requiring empiric antibiotic therapy.[15] According to our findings, 62% of the samples were positive with regard to the level of serum PCT. One-half of those samples (62 people) who was diagnosed to be healthy using VCUG had a normal level of serum PCT. However, 38 people of the samples diagnosed to be healthy using voiding cystourethrogram had a positive result of level of serum PCT.

In other study, only median PCT was significantly higher in patients with renal scar.[22] This study revealed no significant differences in PCT values in children with and in those without VUR and VUR grade.[22] In other study, a meaningful relationship between VUR grade more than 3 and the clinical decision regulation was not found.[19] In children with VUR grade ≥3, PCT is remarkably higher than in children with no or low- grade VUR.[17] The association of PCT with VUR in children with febrile UTI remains controversial. The positive and negative predictive values of the serum level of PCT were 40% and 90%, respectively. In this respect, 50% of the samples diagnosed by serum level of PCT were false positive and 12% were false negative. It meant that sensitivity and specificity of PCT measurement were 90% and 50%, respectively. In other study, it has been reported that PCT is a suitable predictor of cystographic findings and can be substituted with VCUG in some cases of young children with febrile urinary tract infections.[21] The positive predictive value of serum PCT for the female and male samples was 42% and 54% respectively. Nowadays, the evaluation of vesicoureteral reflux is carried out using different imaging methods such as sonography, voiding cystourethrogram (VCUG), and direct radionuclide cystography (DRNC) that are accompanied with different limitations. Pediatricians are looking for other evaluation methods that are feasible, easy to implement and carries the least amount of danger to the patient In this respect, the evaluation of vesicoureteral reflux by using the serum level of PCT as a non- radiological method is suggested. However, one of the limitations of our study was the low number of our cases that limits the widespread of serum level of PCT in the diagnosis of pediatric UTI and VUR.

Conclusion

The present study concluded that the no statistically significant relationship between vesicoureteral reflux and the serum level of PCT. However, due to some limitations in our study, more studies are recommended with more numbers for better determination of

diagnostic values of procalcitonin serum levels in relation to VUR.

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