

Commentary

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Urinary IL-8: As a Noninvasive Biomarker for Diagnosis of Vesicoureteral Reflux in Children

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See article on page 112, Is Urinary Interleukin-8 a Marker of Vesicoureteral Reflux in Children?

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Urinary tract infection (UTI) is one of the most common bacterial diseases in children; it is acquired by an estimated 3-5% of the girls and 1% of the boys. UTI has been considered an important risk factor for the development of progressive renal disease and long-term complications [1,2,3]. Vesicoureteral reflux (VUR) is a common finding in children who develop urinary tract infection (UTI) and prenatally diagnosed urinary tract dilatation as well as the relatives of the index patients. Children with VUR are believed to be at risk for ongoing renal damage with subsequent infections, resulting in hypertension and reduced renal function [1, 2]. VUR has become an exciting area for clinical, basic science, and translational research. The detection of VUR and renal scarring currently depends on imaging modalities with associated problems including radiation, invasiveness, and expenses [4]. Various imaging and biochemical methods with different specificity and sensitivity rates have been introduced as substitute diagnostic tools for VCUG to identify VUR. Cytokines are well known to modulate the inflammatory response in UTI and renal damage.

IL-8, a proinflammatory mediator and a major chemoattractant for neutrophils, is produced by epithelial cells of the renal tract in response to inflammatory stimuli and has been shown to increase during UTI [5,6]. Finally, ongoing basic science research in biomarker discovery (serum basic fibroblast growth factor, procalcitonin, and urine interleukin [7,8], and urinary proteomics are being directed towards the development of new noninvasive tests to diagnose and perhaps prognosticate children with VUR [5,6,7,8]. Several studies in the literature have been performed by researchers from Iran, the Middle East, and other countries regarding the association between urinary IL-8 as a noninvasive biomarker and diagnosis of vesicoureteral reflux in children. Galanakis et al evaluated 59 infants [8] and reported that IL-8 levels were elevated in infants with VUR even in the absence of UTI. Their findings suggest that the cutoff of 5 pg/mol IL 8/creatinine is of high sensitivity and adequate specificity for diagnosing VUR [8]. Shenophy et al reported urinary IL-8 levels were higher in children with VUR even in the absence of UTI [9].

A study by Amal et al revealed that urinary IL-8 levels were significantly elevated in children with VUR [10]. Their research showed that urinary IL-8 seemed to be a promising preliminary diagnostic marker for VUR. Rao et al reported that urine IL-8 was a sensitive but poorly specific test for UTI as it could be found in a variety of other infectious and inflammatory disorders [6]. Merrikhi showed that urinary IL-8 might be helpful in determining high grade VUR, but the results of this study showed that the sensitivity, specificity, PPV, and NPV of this marker were not satisfactory in the cutoff point of 5 pg/Cmol and other variables must be controlled [11]. Mahyar et al [12] showed no significant difference between serum IL-6 and IL-8 concentrations, and the presence and severity of VUR (p value= 0.799).

In this issue of the journal, Seyedzadeh et al evaluated urine levels of IL-8 in 41 children aged 1 to 60 months regarding the association between urinary IL-8 and diagnosis of vesicoureteral reflux and reported no significant difference between urine IL-8/Cr levels in patients with and without VUR; therefore, we cannot propose IL-8 as a diagnostic marker for VUR [13]. In contrast to most previous studies, they reported that urinary IL-8 did not have a practical value in identifying VUR. However, there are some conflicts about this paper that are vague. Much of the discussion is about the relationship of urinary tract infection and IL-8 not VUR. The discussion section should focus on relevant studies in the world, Asia, Middle East, and Iran. The application of statistical methods for analyzing his reported results such as the use of One-Way ANOVA and Tukey's Post Hoc Test as well as Chi-square test is not shown in the manuscript. Moreover, some issues on the details of the patients are not clear; for example, the number of patients with primary or secondary reflux and the difference between the level of IL-8 in these patients. The number of patients with unilateral or bilateral reflux and the severity and grading of VUR in patients are not mentioned, as well. In conclusion, according to the finding of this study, it seems that the validity of urinary IL-8 as a noninvasive biomarker in the diagnosis of vesicoureteral reflux should be substantiated in future studies with more patients and more defined selection criteria with regards to the limitations.

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