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Serum and urinary thioredoxin concentrations are associated with severity of children hydronephrosis

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ABSTRACT

Background: Ureteropelvic junction obstruction (UPJO) is the most common cause of hydronephrosis in children. This study was to assess the relationship between serum thioredoxin (S-Trx) and urinary thioredoxin (U-Trx) concentrations and severity of children hydronephrosis caused by UPJO.

Methods: This study included 156 hydronephrosis children with unilateral UPJO and 80 healthy children. S-Trx and U-Trx concentrations were measured using enzyme-linked immunosorbent assay. U-Trx/creatinine (cr) ratio was calculated.

Results: S-Trx and U-Trx concentrations and U-Trx/cr ratio were significantly higher in hydronephrosis children than in healthy children. They were significantly correlated with split renal function, anterior–posterior diameter and Society for Fetal Urology classification, as well as were independently related to the split renal function <39.2%, anterior–posterior diameter > 30 mm and Society for Fetal Urology grade IV. Under receiver operating characteristic curves, U-Trx/cr ratio showed the higher predictive value compared to S-Trx and U-Trx concentrations.

Conclusion: Increased S-Trx and U-Trx concentrations, especially U-Trx/cr ratio, are closely associated with the severity of children hydronephrosis, substantializing Trx as a promising biomarker for the progression of children hydronephrosis.

1. Introduction

Congenital hydronephrosis (HN) is characterized by distension and dilation of the renal pelvis and calyces due to various congenital obstructive malformations of the kidneys and urinary tract. Ureteropelvic junction obstruction (UPJO) is the most common cause of congenital HN in children [1–3]. HN can evolve into renal agenesis and clinically presents as chronic kidney disease in children [4–6]. Currently, some clinical tests, including renal ultrasonography and radionuclide renography can help to predict the future course of HN and identify patients who require surgical treatment [7–9]. However, these conventional imaging modalities still are insufficient for decision making in managing the condition. In addition, radionuclide renography exposes children to radiation and causes radiation damage. Thus, the interests of clinicians have focused on the potential role of plasma or urine markers in HN [10–12].

HN-caused renal injury is a complex process and its underlying mechanisms involve oxidative stress and inflammation [13–15]. Thioredoxin (Trx), a 12-kDa ubiquitous thiol protein, possesses a potent anti-oxidant effect and modulates inflammation [16–19]. Intracellular Trx is released from cells upon oxidative stress, leading to high extracellular concentrations in a great number of critical illnesses including: severe burn injury, chronic heart failure, acute live injury and sepsis [20–23]. Recently, increased serum Trx concentrations are found to be a diagnostic marker for hepatocellular carcinoma [24], and have close relation with myocardial damage amount in acute myocardial infarction [25]. Moreover, enhanced serum TRX concentrations are correlated significantly with the severity and poor outcome following acute ischemic stroke [26], severe traumatic brain injury [27] and intracerebral hemorrhage [28]. Recently, Trx is found to be increased in urine from mice with acute nephropathy, in which it exerts a protective effect on injured kidney [29,30]. This study was designed to investigate serum Trx (S-Trx) and U-Trx concentrations in children with UPJO-caused HN and further elucidate the relationship between its concentrations and the HN severity.

Abbreviations: Cr, creatinine; Trx, thioredoxin; S-Trx, serum Trx; U-Trx, urinary Trx; HN, hydronephrosis; UPJO, ureteropelvic junction obstruction; eGFR, estimated glomerular filtration rate; APD, anterior–posterior diameter; SRF, split renal function; SFU, Society for Fetal Urology.

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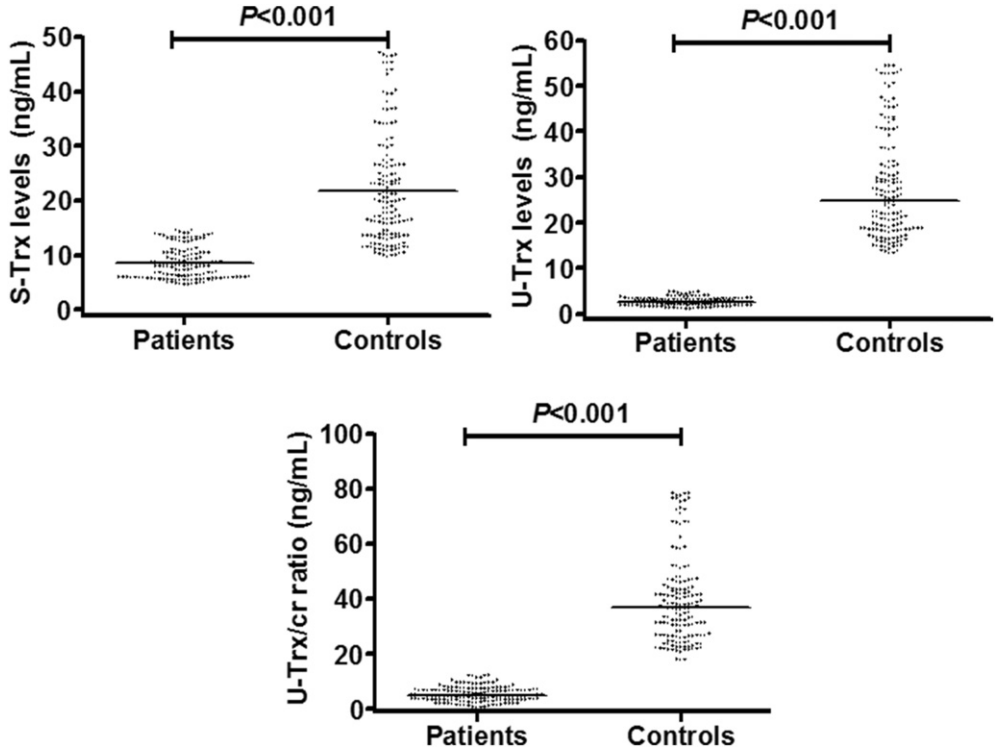

Fig. 1. Intergroup comparisons of serum thioredoxin (S-Trx) and urinary thioredoxin (U-Trx) concentrations as well as U-Trx/creatinine (cr) ratio between controls and hydronephrosis children.

Table 1
Correlative analysis between thioredoxin levels and split renal function and anterior-posterior diameter in hydronephrosis children.

Parameter	Split renal function		Anterior–posterior diameter	
	r value	*P* value	r value	*P* value
S-Trx levels				
Model 1	−0.235	0.003	0.200	0.012
Model 2	−0.209	0.010	0.169	0.037
U-Trx levels				
Model 1	−0.417	<0.001	0.345	<0.001
Model 2	−0.300	<0.001	0.292	<0.001
U-Trx/cr ratio				
Model 1	−0.503	<0.001	0.453	<0.001
Model 2	−0.437	<0.001	0.337	<0.001

In model 1, bivariate correlation analyses were conducted using Spearman"s correlation coefficient. In model 2, partial correlation coefficient was performed for adjustment of age, sex and estimated glomerular filtration rate. S-Trx indicates serum thioredoxin; U-Trx, urinary thioredoxin; cr, creatinine.

2. Materials and methods

2.1. Study population

This was a cross-sectional study carried out between January 2011 and January 2015 at the Children's Hospital, College of Medicine, Zhejiang University, China. We included the children with HN due to unilateral UPJO. We excluded those children with urinary tract infection, vesicoureteral reflux, ureterovesical junction obstruction, posterior urethral valve obstruction, bilateral HN, previous operation on the urinary system, other deformations of the external genital organs, lower urinary tract anomalies, urinary stones and neurogenic bladder dysfunction. The control group was composed of healthy children referred to a pediatric outpatient clinic, where all children are periodically monitored for their development and growth. This study was approved by the ethics committee of our medical faculty. All caregivers of the children were interviewed and gave written informed consent for the children to participate in the study.

Table 2
Independent association of thioredoxin levels with the children hydronephrosis severity.

Parameter	Split renal function <39.2%		Anterior–posterior diameter > 30 mm		Society for Fetal Urology grade IV	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
S-Trx levels						
Model 1	1.063 (1.026–1.102)	0.001	1.034 (1.001–1.069)	0.042	1.035 (1.002–1.069)	0.035
Model 2	1.067 (1.029–1.107)	0.001	1.037 (1.004–1.074)	0.040	1.038 (1.007–1.093)	0.030
U-Trx levels						
Model 1	1.108 (1.066–1.152)	<0.001	1.071 (1.037–1.106)	<0.001	1.072 (1.039–1.106)	<0.001
Model 2	1.104 (1.060–1.148)	<0.001	1.082 (1.047–1.117)	<0.001	1.085 (1.051–1.130)	<0.001
U-Trx/cr ratio						
Model 1	1.172 (1.112–1.236)	<0.001	1.126 (1.080–1.175)	<0.001	1.099 (1.062–1.138)	<0.001
Model 2	1.181 (1.119–1.245)	<0.001	1.133 (1.086–1.189)	<0.001	1.102 (1.073–1.159)	<0.001

Using binary logistic regression analysis, model 1 only included thioredoxin levels as independent variable and model 2 entered thioredoxin levels in addition to age, sex and estimated glomerular filtration rate as independent variables. S-Trx indicates serum thioredoxin; U-Trx, urinary thioredoxin; cr, creatinine.