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Serum and Urine Leptin Concentrations in Children Before and After Treatment of Urinary Tract Infection

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Introduction. Urinary tract infection (UTI) among children is sometimes associated with anorexia and sometimes failure to thrive. Appetite-regulating hormones may be a causative factor. Leptin regulates appetite, food intake, and body weight via hypothalamic melanocortin-4 receptor. Leptin is also a potential cytokine for inflammation. The aim of this study was to evaluate serum and urine leptin before and after treatment of children with UTI.

Materials and Methods. In this before-after study, serum and urine leptin were measured in 40 patients with UTI at admission and 5 days after treatment. Pyelonephritis was suggested by signs and symptoms and confirmed with positive urine culture and dimercaptosuccinic acid renal scintigraphy. Other measurements included urinalysis, urine culture, urine creatinine level, complete blood count, erythrocyte sedimentation rate, C-reactive protein level and serum levels of urea, creatinine, glucose, cholesterol, and triglyceride.

Results. The mean serum leptin level was 6.85 ± 18.90 ng/mL before the treatment and 8.29 ± 18.30 ng/mL after the treatment, the difference of which was not significant (P = .64). There were significant correlations between serum leptin and age, weight, and C-reactive protein. Urine leptin levels were reduced significantly from 0.75 ± 0.82 ng/mL to 0.46 ± 0.27 ng/mL after the treatment (P = .03). A significant correlation was observed between urine leptin level with age and weight.

Conclusions. Serum leptin level did not change significantly after treatment of UTI, but urine leptin significantly decreased. Serum leptin level was higher in patients with anorexia in comparison with children with normal appetite; however, the difference was not significant.

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INTRODUCTION

Leptin is a 16-kD protein encoded by the obese gene in adipose tissue that acts as an anorexigenic hormone and cytokine.[1,2] It suppresses appetite and food intake by hypothalamic melanocortin-4 receptor.[3] As a cytokine, an association between serum leptin level and C-reactive protein (CRP) was demonstrated, serving in the regulation of immune function by thymic homeostasis.[4] Furthermore, leptin is excreted by glomerular filtration and then degradated by the renal tubules. Therefore, serum leptin level is increased in patients with chronic kidney disease and hemodialysis patients.[3,5-8]

There has been many efforts to identify the

mechanisms of renal injury, diagnosis and underlying conditions of pyelonephritis, and treatment and prognosis of pyelonephritis.[9-17] In recent years, many investigators identified alterations of leptin level in various conditions such as chronic kidney disease, infections, severe sepsis, nephritic syndrome, cardio metabolic risks, and colonic diseases.[18-30] Furthermore, based on animal studies, other functions have been suggested for leptin, such as angiogenesis, activation of T lymphocyte, production of transforming growth factor-β, glomerulosclerosis, as well as induction of oxidative stress, wound healing, and hypertension.[4,31-35] Further investigations may identify its role in these conditions.

Urinary tract infection (UTI) is one of the most common infections in infancy and childhood. Its manifestations varies from fever, poor feeding, or failure to thrive (FTT) in infants to urinary symptoms and poor weight gain in older children. In the present study, we investigated serum and urine leptin concentrations before and after treatment of UTI and its potential association with FTT and induction of renal scars.

MATERIAL AND METHODS

A total of 40 patients admitted with UTI to the Department of Pediatric Nephrology were included in the study. Pyelonephritis was suggested based on the signs and symptoms as well as a positive urine culture, and it was confirmed with the findings of photopenic areas in dimercaptosuccinic acid (DMSA) renal scintigraphy. Exclusion criteria were negative urine culture, no evidence of pyelonephritis on DMSA scan, systemic diseases, and chronic kidney disease.

Before treatment, urine and blood samples were collected and stored at -20°C for measurement of leptin. Other measurements included urinalysis, urine culture, urine creatinine level, complete blood count, erythrocyte sedimentation rate, CRP level and serum levels of urea, creatinine, glucose, cholesterol, and triglyceride. On the 5th day of admission, samplings for the abovementioned tests were repeated. Other investigations were ultrasonography, voiding cystourethrography, and DMSA renal scintigraphy. At the end of the study, serum and urine samples were analyzed with the Mediagnost human leptin enzyme-linked immunosorbent assay E07 kits (Reutlingen, Germany) with 0.2 ng/mL sensitivity.

Statistical analyses were performed using the paired *t* test for quantitative data and the Wilcoxon test for qualitative data. Correlations were examined using the Spearman coefficient. A *P* value less than .05 was considered significant.

RESULTS

Forty patients including 35 girls (87.5%) and 5 boys (12.5%) were studied. The mean values for age, weight, and body mass index were 48.3 ± 46.1 months (range, 2 to 162 months), 17.0 ± 10.7 kg (range, 4.5 kg to 51 kg), and 15.5 ± 1.9 kg/m^2 (range, 12 kg/m^2 to 20 kg/m^2), respectively. Based on ultrasonographic studies, hydronephrosis was detected in 8 patients (20.5%). In 29 patients, voiding cystourethrography was performed which showed vesicoureteral reflux in 9 (31.0%), including 4 bilateral and 5 unilateral. The DMSA scans revealed pyelonephritis (reduced uptake in 1 to 2 poles) in 22 patients (66.7%) and multiple areas suspected to lead to scar formation in 9 (27.3%).

The mean serum leptin level was 6.85 ± 18.90 ng/mL (range, 1.0 ng/mL to 100.0 ng/mL) before the treatment and 8.29 ± 18.30 ng/mL (range, 1.0 ng/mL to 79.3 ng/mL) after the treatment, the difference of which was not significant (*P* = .64). There was a significant correlation between serum leptin and age, weight, and CRP as is shown in the Table, but no significant correlation with other variables. Serum leptin level was not associated with the presence of pyelonephritis, hydronephrosis, vesicoureteral reflux, weight loss, or history of UTI, either. Serum leptin levels were higher in the patients with anorexia as compared to the patients with normal appetite, but the difference was not significant (8.32 ± 23.6 ng/mL versus 5.06 ± 11.3 ng/mL, *P* = .59). No correlation was seen between serum leptin levels and renal scar (18.2 ± 35.7 ng/mL versus 1.08 ± 0.11 ng/mL, *P* = .26).

Urine leptin levels were reduced significantly after the treatment (*P* = .03); The mean urine leptin level was 0.75 ± 0.82 ng/mL (range, 0.18 ng/mL to 5.70 ng/mL) before the treatment and 0.46 ± 0.27 ng/mL (range, 0.05 ng/mL to 1.64 ng/mL) after the treatment. Also, a significant correlation was observed between urine leptin level with age and weight (Table). The mean urine leptin was higher in those patients with pyelonephritis who developed renal scar (Figure 1); however, the difference

Correlation Between Serum and Urine Leptin Values and Quantitative Variables in 40 Children With Urinary Tract Infection (UTI)

Parameters	Serum leptin		Urine Leptin	
	Correlation Coefficient	*P*	Correlation Coefficient	*P*
Age	0.40	.01	0.33	.03
Body weight	0.44	.004	0.31	.049
Body mass index	0.26	.10	0.09	.54
Duration of UTI	0.08	.62	0.04	.82
Proteinuria	0.12	.45	-0.05	.76
Erythrocyte sedimentation rate	-0.06	.70	0.03	.85
C-reactive protein	-0.31	.05	0.07	.60
Cholesterol	0.02	.89	0.06	.69
Triglyceride	0.05	.76	-0.03	.89
Blood glucose	0.04	.79	-0.10	.52

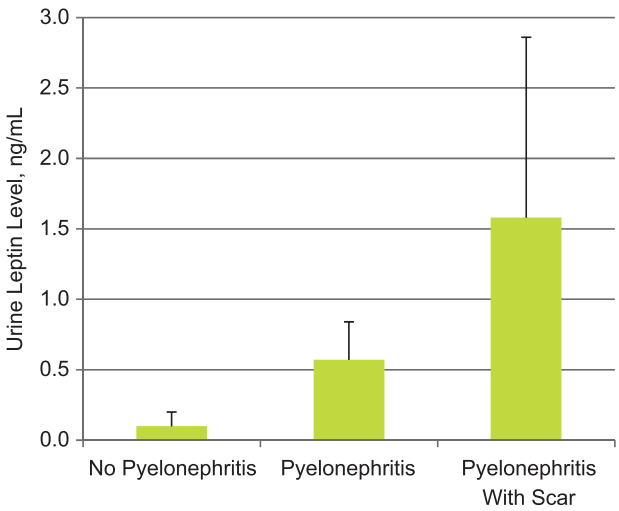

Figure 1. Mean serum leptin levels by pyelonephritis and its scar formation

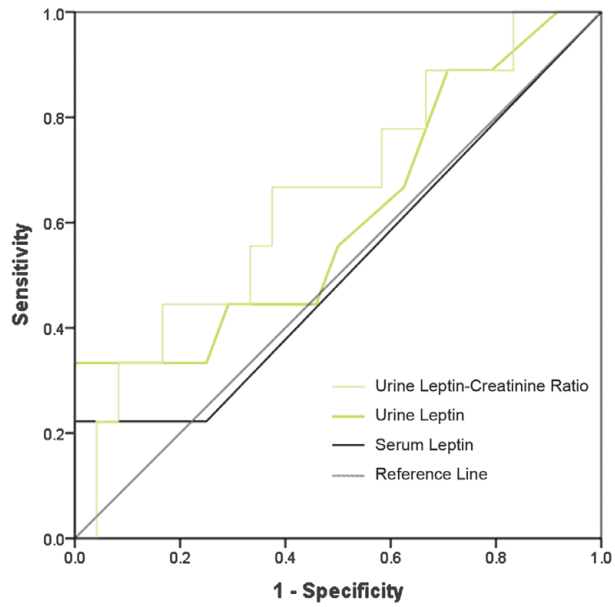

Figure 2. Sensitivity and specificity of serum leptin, urine leptin and urine leptin-creatinine ratio before treatment for detecting kidney scar in 40 children with urinary tract infection.

was not significant. Urine leptin level was not associated with the presence of pyelonephritis, hydronephrosis, vesicoureteral reflux, weight loss, or history of UTI, either.

Urine leptin-creatinine ratio revealed no significant difference before and after treatment (P = .68). Diagnostic value of serum leptin, urine leptin, and urine leptin-creatinine ratio for detecting renal scar were studied by the receiver operating characteristic curve (Figure 2) that showed no significant value (area under the curves, 0.514 ± 0.121, 0.611 ± 0.118, and 0.650 ± 0.109, respectively; P = .90, P = .33, and P = .18, respectively).

DISCUSSION

In this study, we investigated serum and urine leptin before and after treatment of UTI in 40 pediatric patients and their association with renal scar and inflammatory markers. Serum and urine leptin showed positive correlation with weight and age and negative correlation with CRP and no correlation with renal scars or vesicoureteral reflux. Urine leptin decreased significantly after treatment, but serum leptin did not show this difference.

To our knowledge this is the first study that investigates serum and urine leptin in pediatric UTI. There are considerable number of articles on the role of leptin in renal diseases including development of proteinuria, focal glomerulosclerosis, natriuresis, increased sympathetic activity, and induction of reactive oxygen species, and its relationship with inflammation and cytokines such as tumor necrosis

factor-α and interleukin-6.[36,37] On the other hand, alteration of cytokines in UTI and renal scars is revealed by some researchers.[38]

In Militsi and colleagues' study,[39] there was a significant correlation between serum leptin, CRP, and procalcitonin before and after treatment of minor infections. Thus, based on these results, leptin was considered as an acute-phase reactant. Similarly, serum leptin showed a significant correlation with CRP in Somech and colleagues' study.[4] In our study, leptin had significant correlations with age and weight. Hence, some of these differences could be related to a wide range of age and weight in our patients.

The present study revealed a significant decrease of urine leptin before and after UTI treatment that was not investigated before. Wasilewska and coworkers showed increased urine but not serum leptin in children with nephritic syndrome.[40] Significant decreases in urine leptin in our study may be due to degrees of proteinuria or alteration in its renal metabolism in children with UTI; this could be investigated by further studies.

CONCLUSIONS

We found positive correlations between serum leptin and CRP and a significant decrease in urine leptin with treatment of UTI. This reveals that alterations of serum and urine leptin need further investigation in patients with UTI. Further studies with greater number of patients are required to achieve more definite results.

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CONFLICT OF INTEREST

None declared.

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