Correlation of Sacral Ratio and Reflux-Related Renal Injury in Children with Vesicoureteral reflux with and without Nephropathy

Introduction: Vesicoureteral reflux refers to the retrograde flow of the urine from the bladder to the ureter and kidney. The ureteral attachment to the bladder is normally oblique, between the bladder mucosa and detrusor muscle, creating a flap-value mechanism that prevents reflux. Reflux occurs when the submucosal tunnel between the mucosa and detrusor muscle is short or absent. The inflammatory reaction caused by pyelonephritis can result in scarring, which is also termed reflux nephropathy. Since sacral bone anomalies have a direct influence on the final function of the urinary and bowel systems, this study was performed to investigate the relationship between sacral ratio and reflux nephropathy.

Materials and Methods: In this case-control study, the case-control group included 200 children under 9 years old who were referred to Amir-Kabir Hospital clinics with urinary tract infection and according to the VCU and DMSA results, children with various grades of VUR entered the study. The sacral ratio was measured in the two groups and compared by a radiologist. The data were analyzed using Chi-2 and Mann Whitney Tests and software SPSS 16.

Results: The case group included 48 males and 52 females with a mean age of 3.7 years old who had reflux nephropathy, and the control group included 47 males and 53 females with a mean age of 4.1 years who did not have reflux nephropathy. Sacral ratio abnormality was detected in 64% and 23.7% of the cases and controls respectively, which showed a significant difference (p-value=0.003).

Conclusions: Sacral ratio abnormality was more common in children with vesicoureteral reflux and reflux nephropathy than children with VUR without reflux nephropathy.

Keywords: Vesico-Ureteral Reflux; Sacral agenesis; Child; Diagnostic imaging.

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Introduction
Reflux predisposes the kidneys to infection (pyelonephritis) through facilitating the transport of bacteria from the bladder to the upper urinary tract [1]. The inflammatory reaction caused by pyelonephritis can result in kidney injury or scarring, which is also termed reflux-related renal injury or reflux nephropathy. In pediatric patients with a febrile urinary tract infection (UTI), those with vesicoureteral reflux are 3 times more likely to develop kidney injury compared to those without reflux [2]. DMSA is a renal cortical imaging agent which is used to assess the
differential renal function and to demonstrate whether kidney scarring is present. Extensive renal scarring impairs renal function and can result in renin-mediated hypertension, renal insufficiency or end-stage renal disease, impaired somatic growth, and morbidity during pregnancy [3]. The severity of reflux is graded using the International Reflux Study Classification of 1 to 5 based on the appearance of the urinary tract on a contrast voiding Cystourethrogram (VCUG).

Grading of reflux is follows:
Grade 1: reflux into a no dilated ureter
Grade 2: reflux into the upper collecting system without dilatation
Grade 3: reflux into dilated ureter and/or blunting of calyceal fornices
Grade 4: reflux into grossly dilated ureter
Grade 5: massive reflux, with significant ureteral dilatation and tortuosity and loss of the papillary impression [4].

Sacrum anomalies like hypoplasia (which is underdevelopment of the sacrum) or aplasia (which is congenital lack of sacrum) are accompanied by urinary disorders. Today, the association of sacral agenesis and neuropathic bladder, voiding dysfunction with or without secondary reflux, is well known [5]. The anatomical proximity of sacrum and distal ureters might fabricate co-occurrence of developmental abnormalities in both organs [6-8]. Although plain radiograms are used to investigate bony sacral abnormalities, it can be difficult to assess them. In 1995, Pena introduced sacral ratio (SR) as a novel method to evaluate bony indexes of the sacrum as a predictive value of anorectal malformations and voiding dysfunction [3]. It has been used by several other investigators thereafter. Due to the limited research in this regard, this study was performed to evaluate the relationship between sacral ratio and primary YUR with and without reflux nephropathy.

Materials and Methods
In this study, we evaluated children aged 3-9 years old who were visited in pediatric nephrology clinics of Amir-Kabir Hospital, Arak, Iran, between March 2009 to March 2012. The age of 9 years old was selected as the maximum age due to the changes in the sacral ratio after the puberty. The case group included 100 children under 9 years old with UTI. According to VCUG and Dimercaptosuccinic acid renal scan (DMSA), children with VUR and photopenic areas including acute pyelonephritis and renal scaring entered the study (reflux nephropathy was documented with repeating DMSA 4 to 6 months after acute UTI). The control group included 100 children with similar demographic information with VUR who had normal DMSA results 4 to 6 months after acute UTI. To calculate the sacral ratio, anteroposterior (AP) pelvic radiograms were used. Three lines were drawn for each radiograph (X= a horizontal line connecting the uppermost parts of the iliac crest of both sides, Y= a horizontal line connecting the lowermost parts of sacroiliac joints of both sides, Z= a horizontal line passing the lowermost part of the sacrum). If all the lines were not parallel to each other, we excluded the patient from the study. SR was defined as the proportion of YZ to XY (SR=YZ/XY). Pena described the normal limits of SR as >0.74 in AP and >0.77 in lateral views [3]. All radiographic images were obtained and assessed by the same radiologist. Therefore, to have high quality radiograms for detecting the tip of the sacrum, a direct digital radiography system was used in most of the patients. Since obtaining the lateral view meant additional X-ray exposure, the study was restricted to assessing the SR ratio in the AP view. Statistical analysis of data was performed using SPSS 16.0 for Windows. Mean values and standard deviation were calculated for all groups. Chi-square was applied to compute the significance of the categorical variables and p <0.05 was considered significant.

Results
The case group included 48 males and 52 females with a mean age of 3.7 years and the control group
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included 47 males and 53 females with a mean age of 4.1 years. SR abnormality was detected in 64% and 23.7% of the cases and controls respectively, which showed a significant difference (P-value=0.003).

Discussion
In this study we compared the SRs of 200 children with and without reflux nephropathy. There was an apparent relation between mean SR of both groups. This finding was similar to the results of a study by Kajbafzadeh et al who compared SRs of children with and without urinary and fecal complaints. In their case group, SR abnormality was observed in 13.2% and 13.3% of the patients with urinary and fecal complaints respectively while it was detected in 0.5% of the patients in the control group. Therefore, SR was introduced as a valuable index for prediction of urinary or fecal complaints [6]. Warne evaluated 50 pelvic radiographs of children with anorectal abnormality and 20 healthy children and concluded that SR was a good measure for sacral development; however, the range of SRs they used was too wide to differentiate between normal and abnormal SRs [7]. KhaleghNejad suggested that SR was a good predictor of fecal continence after colorectal surgery and a valuable index for sacral development [9]. Kajbafzadeh reported that SR could be considered as a reliable tool to evaluate sacral development in patients with urinary and/or fecal complaints [10]. Yousefichaijan stated that SR could be used in the determination of the prognosis of medical treatment considering the significant relationship between the normal of sacrum index and urinary reflux [11]. However, according to the results of a study by Basiratnia, it is not still clear to what extent the SR could be used as an indicator of VUR [12]. The reason for difference in these reports could be the heterogeneous populations enrolled in the mentioned studies.

Conclusions
This study showed an apparent correlation between reflux nephropathy and SR, which can be used as a predictive factor in the determination of the prognosis of medical treatment and selecting the children for surgery. A multicenter study with a larger sample size is suggested to investigate the correlation between reflux nephropathy and SR.

Conflict of Interest
None declared

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None declared

References