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The Relationship Between Prenatal Hydronephrosis and Vesicoureteral Reflux in Children With a History of Prenatal Hydronephrosis in the Third Trimester of Pregnancy

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ABSTRACT

Background and Aim: Prenatal hydronephrosis is found in 1%-5% of pregnancies. Without well-timed diagnosis and treatment, it can lead to irreversible outcomes. Because little information is available on the indication of Vesicoureteral Reflux (VUR) regarding the antenatal diameter of the kidney pelvis, the current study aimed to determine the association between prenatal hydronephrosis and the VUR.

Methods: This cross-sectional study was conducted from 2011 to 2016 on 200 neonates with hydronephrosis detected in fetal life ultrasounds in the third trimester of pregnancy. We assessed the prenatal and postnatal kidney ultrasonography of 400 kidneys and Voiding Cystourethrogram (VCUG). We employed the Spearman correlation coefficient for determining the association between study variables. The obtained data were analyzed using SPSS 16.0 software at a significance level of less than 0.05.

Results: Of 200 infants, 71.5% were males and 28.5% were females. No significant relationship was found between the degree of antenatal hydronephrosis and the VCUG severity (r=0.098, P=0.106). Despite antenatal hydronephrosis, the degree of postnatal hydronephrosis and the VCUG severity was correlated (r= 0.255, P=0.001).

Conclusion: There is no correlation between the severity of fetal hydronephrosis and VUR severity or the presence of a greater correlation between postnatal hydronephrosis and degree of VUR. Thus in cases of mild prenatal hydronephrosis, we suggest urinary tract ultrasonography three to seven days after birth and then cystography if postnatal sonography showed moderate or severe or progressive hydronephrosis.

Keywords: Hydronephrosis, Pyonephrosis, Congenital, Urinary tract infection, Child, Vesicoureteral reflux, Cystography

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Introduction

Prenatal screening is an essential part of prenatal care. Nearly 1% of fetuses have anomalies, among which one-fifth are genitourinary abnormalities [1]. Antenatal hydronephrosis is seen in 1% to 5% of cases. It has several differential diagnoses, such as Vesicoureteral Reflux (VUR), Ureterovesical Junction (UVJ) stenosis, Ureteropelvic Junction (UPJ) stenosis, and Posterior Urethral Valve (PUV) obstruction. The problem may be a transient phenomenon. Lack of prompt diagnosis and treatment would result in nephrolithiasis, urinary tract infection, kidney scarring, hypertension, and occasionally impaired renal function. It may be categorized based on Anteroposterior Diameter (APD) of the renal pelvis [2] or a 0 to 5 grade according to the Society For Fetal Urology [3]. In a study on 213 cases with minor degrees of fetal renal pelvis dilatation, 62% had uropathy, of which 39% were significant. The predictive ability of renal pelvis dilation for genitourinary tract anomalies was 12% in the second trimester and 69% in the third trimester [4]. Although some laboratory or clinical factors could be independent predictors of the VUR presence [5, 6], hydronephrosis has been considered the most related factor in studies.

Patients with high-grade reflux are more likely to have more severe hydronephrosis. Approximately 10%–30% of patients with prenatal hydronephrosis and 30%–35% of patients with severe prenatal hydronephrosis will have primary VUR [7, 8]. It is impractical to predict reflux or its grade by prenatal imaging. Moreover, while VUR can appear as hydronephrosis on prenatal sonography, there are no specific signs to point its presence. Postnatal ultrasonography can be normal in patients with prenatal hydronephrosis due to VUR. After all, one study showed that the 27th percentile of patients with prenatal hydronephrosis and grade 2 to 5 VUR had normal postnatal sonography [9, 10]. Prophylactic antibiotics have demonstrated the potential to cut back severe urinary tract infections in children with VUR. Delayed diagnosis of VUR may result in irreversible outcomes.

Due to the contradictory results in the relationship between renal pelvis anteroposterior diameter and grade of VUR, we decided to do this study. These steps may be taken before deciding definitive management for a given patient.

Because of the limited evidence on the indication of cystography based on the antenatal diameter of the renal pelvis, the current study aimed to determine the association between the severity of prenatal hydronephrosis and the VUR severity.

Materials and Methods

Data of this study were collected from 200 infants with a history of fetal hydronephrosis in the third trimester of pregnancy who underwent renal sonography in the first seven days of their lives and cystography in infancy. The exclusion criteria were the presence of other anomalies in fetal ultrasound, presence of single or ectopic kidney, meningomyelocele, lack of third-trimester ultrasound assessment, ambiguous genitalia, neonatal intensive care unit admission, or lack of follow-up after the birth.

The current study was approved by the local Ethics Committee and the ethical code of IR.SBMU.MSP.REC.1396.355 was attained from Shahid Beheshti University of Medical Sciences, Tehran, Iran. The study data were recorded on a checklist and included maternal age, neonatal sex, gestational age at ultrasonography, and ultrasound variables, including Anteroposterior Diameter (APD) in the right and left pelvis before and after birth, DTPA (Diethylene-Triamine-Pentaacetate) scan, and Voiding Cystourethrogram (VCUG) or isotope cystography results.

APD of the renal pelvis was divided into quartiles and four groups based on the assessment of the kidney pelvis cognate with cut-off points reported in previous clinical studies (Table 1) [11-13].

Reflux grades are 1 to 5, according to Nelson's textbook of pediatrics. Grade 1 is VUR into a no dilated ureter. Grade 2 refers to VUR into the upper collecting system without dilation. Grade 3 is VUR into the dilated ureter and or blunting of calyceal fornices, and grade 4 is VUR into a grossly dilated ureter. Finally, grade 5 refers to a massive VUR with significant ureter dilation and tortuosity and loss of the papillary impression. We consider VUR grade 1 and 2 in standard cystography as mild, VUR grade 3 moderate, and VUR grades 4 and 5 severe.

Data analysis was carried out using SPSS v. 16 software. The Chi-square, Spearman correlation, Kruskal-Wallis, Mann-Whitney, and Independent sample t tests were used for data analysis. P values less than 0.05 were considered significant.

Table 1. Grading of hydronephrosis according anteroposterior Diameter of Renal Pelvis

Hydronephrosis Grade	Anteroposterior Diameter of Renal Pelvis (mm)
Normal	0-4
Mild	5-9
Moderate	9-14
Severe	>15

Results

Among 200 cases studied, 143 neonates (71.5%) were male. Among 400 kidneys, 276 (69%) had fetal hydronephrosis. Differential distributions in two sides are shown in Table 2 (P=0.002). According to Table 2, the prevalence of hydronephrosis was higher in the right kidney, but severe hydronephrosis was more common in the left kidney. The rates of severe hydronephrosis were 11.5% and 6% in the left and right kidneys, respectively. Only 244 kidney units had DTPA results showing obstruction in 39.5% that was complete in 5.8%. The most common obstruction sites were the ureteropelvic junction (72.2%) and the ureterovesical junction (25.8%).

As shown in Table 3, there was no significant association between prenatal hydronephrosis severity and VUR severity in VCUG (P=0.184), but the severity of postnatal hydronephrosis was related to the VUR grade (Table 4) (P=0.002).

In total, 102 kidneys had hydronephrosis both before and after birth. Among 35 cases with severe prenatal hydronephrosis, all but two had postnatal hydronephrosis, which was severe in 51.4% of cases.

Ismaili et al. reported a reflux rate of 9% in cases of acute hydronephrosis, among which 26% were high-grade [14]. Hydronephrosis grading is not always related to VUR severity, but VUR probability in low-grade hydronephrosis cases ranges from 8.5% to 15% [15].

In Sharifian et al.'s study [16], all neonates with hydronephrosis were followed after birth. Ultrasonography showed that 23% of them required surgery with an APD cut-off point of 15 mm that demonstrated a sensitivity and specificity of 95.2% and 73%, respectively. In another study, the outcome of resolved prenatal hydronephrosis was compared to those associated with persistent prenatal hydronephrosis. Recurrent postnatal hydronephrosis occurred in 44% of patients with resolved prenatal hydronephrosis. In comparison, 29% of persistent prenatal hydronephrosis cases resolved postnatally [17]. Sinha A et al. showed that a postnatal APD of more than 10 mm or hydronephrosis grades of 3 and 4 were the appropriate limits for VCUG and obstruction rule-out [18].

In the Grazioli et al. study [19], the fetal ultrasound efficiency was assessed to determine VUR. It was found that VUR risk was increased parallel with APD in the ultrasound imaging (P=0.03). These results are not congruent with the current findings. Phan et al. [7] assessed the correlation between fetal hydronephrosis severity and VUR grade in 111 children. They found that these entities were not correlated (P=0.567). Accordingly, it was mentioned that prenatal hydronephrosis is not a reliable test for determining VUR in children. These results were in agreement with the current findings.

Table 2. Hydronephrosis grading in two sides

Variable	Without Hydronephrosis	No. (%)			
		Hydronephrosis			
		Mild	Moderate	Severe	P
Right kidney	77(38.5)	75(37.5)	36(18)	12(6)	
Left kidney	47(23.5)	100(50)	30(15)	23(11.5)	0.002
Both kidneys	124(31)	175(43.8)	66(16.5)	35(8.8)	

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Table 3. Vesicoureteral Reflux (VUR) grading according to prenatal hydronephrosis

Variables	No. (%)			
	Without Reflux	VUR in Cystography		
		Mild	Moderate	Severe
Without Hydronephrosis	99(79.8)	14(11.3)	7(5.6)	4(3.2)
Mild	11(62.9)	31(17.7)	15(8.6)	19(10.9)
Moderate	37(56.1)	17(25.8)	8(12.1)	4(6.1)
Severe	16(45.7)	11(31.4)	2(5.7)	6(17.1)
P	0.184			

Table 4. Cystogarphy findings in infant with prenatal hydronephrosis

Variable	No. (%)			
	VUR in Cystography	Without Reflux		
		Mild	Moderate	Severe
Without hydronephrosis	95(79.9)	16(13.5)	7(5.9)	1(0.8)
Mild	92(71.3)	16(12.4)	9(7.0)	12(9.3)
Moderate	57(57)	24(24.0)	10(10.0)	9(9.0)
Severe	18(34.6)	17(32.7)	6(11.5)	11(21.2)
P	0.002			

A study of 202 neonates by Mohammadjafari et al. [20] revealed that VUR was correlated to the severity of hydronephrosis. They recommended that VCUG be used in all neonates with antenatal hydronephrosis. Different results were achieved in the current study. Hwang et al. [21] assessed 195 patients and found that VUR is unrelated to antenatal hydronephrosis. The most common cause of antenatal hydronephrosis was ureteropelvic junction obstruction.

In Sadeghi-Bojd et al.'s study on postnatal evaluation and outcomes of prenatal hydronephrosis, a direct relationship was found between APD of the renal pelvis and paroxysmal nocturnal hemoglobinuria consequence. About 20.82% of 167 patients had VUR. The best cut-off point of anteroposterior pelvis diameter of kidneys resulting in operation was 15 mm with a sensitivity of 88% and specificity of 74% [22].

Garcia Nieto et al. investigated whether a bladder contrast imaging should be done for all infants who have mild to moderate distention of the urinary tract system and if kidney function tests could help answer this question. Seventy-nine infants (57 males, 22 females) with pyelectasis were enrolled in this study. Seventy-three were diagnosed in fetal life, and 6 after birth. All infants underwent at least one desmopressin urine concentration exam and one cystography during the first year of age. The research was done to show whether kidney function tests can be used to determine which cases with mild to moderate distention of the urinary tract do not need the earliest bladder contrast imaging. Only two cases needed drug therapy (prophylactic treatment for VUR grade 4 cases). Cystography should not initially be indicated in patients with microalbuminuria and or normal urine osmolality [23].

Sencan et al. evaluated the incidence of urinary tract infection and VUR in children with mild Antenatal Hy-

dronephrosis (ANH) to indicate the need for antibiotic prophylaxis and VCUG. They assessed the information of 1511 cases with various grades of ANH referring to the Department of Urology, Boston Children's Hospital, from January 1998 to January 2010, and 760 cases with mild antenatal hydronephrosis were distinguished. In this study, the prevalence of urinary tract infection and VUR in children with mild antenatal hydronephrosis were low. Accordingly, routine VCUG screening for VUR and using long-term antibiotic prophylaxis was determined not to be suggested for all children who had asymptomatic mild AHN. VUR assessment in children with mild antenatal hydronephrosis should be considered for cases presenting with urinary tract infection [24].

Visuri et al. evaluated whether grade 4 to 5 VUR is predictable from Renal Ultrasound (RUS) results and carried out VCUG only on high-risk cases. They reviewed RUS and VCUG images related to infants with prenatal hydronephrosis referring to their institution between 2003 and 2013. They collected urinary tract infection episodes retrospectively using the patients' files. They omitted those indicating complex urinary tract anomalies. One hundred and eighty patients (44 females and 136 males) (352 Renal Units [RU]) were included in this study, and 23 (30 RU) of them had grade 4-5 VUR. In neonates with antenatal hydronephrosis, a dilated ureter and decreased renal size in RUS are important risk factors for high-grade VUR. A risk scoring according to renal ultrasonography can reduce the request of unnecessary VCUGs [15].

Conclusion

There is no correlation between the severity of fetal hydronephrosis and VUR severity or the presence of a greater correlation between postnatal hydronephrosis and degree of VUR. Considering the prevalence and importance of this issue and the controversial results in different studies, a systematic review should be done regarding the association between the severity of fetal hydronephrosis and the severity of urinary reflux.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished, and if desired, the research results would be available to them. A written consent has been obtained from the subjects. principles of the Helsinki Convention was also observed.

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Authors' contributions

Conceptualization & methodology: Abbas Madani; Validation software: Pegah Meshki; Formal analysis, research, resources, data management, writing: Zahra Pournasiri; Prepare the original draft: Athena Seifi; Review and edit: Ramin Pourian; Visualization, monitoring, project management: Mohammad Amin Shahrbaf.

Conflict of interest

The authors declared no conflict of interest.

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