Review Article Effects of prenatal ultrasonographic imaging feature analysis on diagnostic accuracy of fetal urethral diseases

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Abstract: Objective: To determine the effect of prenatal ultrasonography on the diagnostic accuracy of hypospadias and posterior urethral valve in fetuses. Methods: A total of 58 women with singleton pregnancy whose fetus was diagnosed with suspected urinary system anomalies by prenatal ultrasonography in our hospital from February 2018 to November 2019 were enrolled, of which 30 patients were diagnosed with suspected hypospadias and 28 patients were diagnosed with suspected posterior urethral valve. The ultrasonographic imaging features of fetal hypospadias and posterior urethral valve, and the diagnostic value of prenatal ultrasonography for the two diseases were analyzed. Results: There were 26 cases diagnosed with hypospadias and 25 cases diagnosed with posterior urethral valve after natural or induced delivery. Based on the ultrasonographic imaging features, among fetuses with hypospadias, the occurrence rate of small and short penis was the highest and the correct detection rate of paruria and urethra continuity interruption was the highest. A total of 19 fetuses were diagnosed with hypospadias according to ultrasonography, and the sensitivity, specificity, diagnostic coincidence rate, and positive predictive value of ultrasonography in diagnosing fetal hypospadias were 65.38%, 50.00%, 63.33%, and 89.47%, respectively. Based on the ultrasonographic imaging features, for fetuses with posterior urethral valve, the occurrence rate and correct detection rate of cystauxe were both high. A total of 20 fetuses were diagnosed with posterior urethral valve according to ultrasonography, and the sensitivity, specificity, diagnostic coincidence rate, and positive predictive value of ultrasonography in diagnosing posterior urethral valve were 72.00%, 66.67%, 71.43%, and 94.74%, respectively. Conclusion: Prenatal ultrasonography has high sensitivity and positive predictive value in diagnosing hypospadias and posterior urethral valve, although its specificity in diagnosing them is not always high. Therefore, prenatal ultrasonography can be adopted as a reference for prenatal examination.

Keywords: Prenatal, ultrasonograpic imaging, fetus, hypospadias, posterior urethral valve

Introduction

In recent years, with the toxification of the environment and the changes in people's modern life styles, the incidence of congenital diseases in fetuses has increased worldwide, causing serious burden to families and society overall [1]. According to statistics [2], congenital abnormalities account for 8.9% and 8.0% of all fetal deaths (over 22 weeks old) in the Republic of Korea and Japan, respectively; and the incidence of urinary diseases is relatively high. The fetal urinary system is developed from the intermediate mesoderm at the lateral side of the body segment, during which abnormal development of the system may result in various urinary system malformations [3]. Fetal urinary system malformation, has an incidence reaching 0.2%-0.5%, is a common fetal malformation, which accounts for approximately 20% of all the various system malformations, and its inducing factors include the environment and heredity [4, 5]. Urinary system malformation includes renal dysplasia and urethral malformations, among which urethral malformations include hypospadias and posterior urethral valve [6]. Hypospadias refers to the abnormal position of the urethral orifice in the penis, scrotum abdomen or perineum, and it is a common malformation of the urinary system found

in children. It's etiology is unknown, and its known risk factors include premature delivery, fetal growth restriction, and maternal smoking [7]. Dave S et al. [8] have pointed out that the incidence of hypospadias is about 3.8/1000 in cases of newborn males (live births). Chen MJ et al. [9] have also pointed out that in 2012, the prevalence rate of hypospadias in the United States increased from 6.1 to 6.8 per 1000 newborn babies. The incidence rate of congenital lower urinary tract obstruction is 2.2/1000, and posterior urethral valve is the most common congenital lower urinary tract obstruction, accounting for about 64% of lower urinary tract obstructions [10]. Patients with posterior urethral valve are mostly males [11]. Hypospadias and posterior urethral valve pose a certain threat to patients' physical and mental health. For example, hypospadias exerts a severe impact on the future reproductive function of children, and posterior urethral valve is prone to bring bout secondary chronic kidney disease [12, 13]. At present, some reports and studies have confirmed that intervention during pregnancy can benefit fetuses in perinatal survival [14]. Therefore, it is of great significance to effectively and accurately diagnose the patients and treat them accordingly. As medical imaging technology develops, great progress has been achieved in ultrasound technology. Ultrasound technology is noninvasive, convenient, and accurate in diagnosing diseases. This study analyzed the accuracy of prenatal ultrasonographic imaging feature-based diagnosis in fetal urethral diseases (hypospadias and posterior urethral valve), with the goal of providing relevant references and guidance for future clinical analysis and diagnosis of such diseases.

Materials and methods

General materials

A total of 58 women (average age of (27.08± 4.13) years) with a singleton pregnancy whose fetus was diagnosed with suspected urinary system anomalies according to prenatal ultrasonography in our hospital from February 2018 to November 2019 were enrolled, of which 30 patients were diagnosed with suspected hypospadias and 28 patients were diagnosed with suspected posterior urethral valve. This experiment was approved by the Ethics Committee of our hospital, and all research subjects signed informed consent forms.

Inclusion and exclusion criteria

The inclusion criteria of the study: Women with singleton pregnancy whose fetus was diagnosed with suspected urinary system anomalies according to ultrasonography. The exclusion criteria of the study: Women with multiple pregnancies, pregnant women comorbid with severe hepatic or kidney function obstacles, pregnant women with mental disease who were not able to cooperate with the examination, pregnant women without complete clinical data, and referred pregnant women.

Methods

Each pregnant woman was examined using a GE Voluson E8 color Doppler ultrasonic diagnostic apparatus in a supine position or lateral position, with the probe frequency adjusted to 3.5-7.5 MHz. The fetal genitals were analyzed in terms of penis size, morphology, urethral continuity, and normality of the urinary stream. For fetuses suspected with a lower urinary tract obstruction, their bladder size was dynamically monitored, and their greatest diameter of the bladder and degree of bilateral hydronephrosis were analyzed and recorded. If an abnormality was found by two-dimensional ultrasonography, three-dimensional ultrasonography was carried out, if necessary. The ultrasonography results were compared with clinical follow-up results after natural delivery or inducted delivery. The results of postpartum examination or autopsy were also compared with the prenatal ultrasonography-based diagnosis results, and analyzed. The diagnostic sensitivity = the number of patients with true positive result/(the number of patients with true positive result + the number of patients with false negative result) ×100%. The diagnostic specificity = the number of patients with true negative result/ (the number of patients with false positive result + the number of patients with true negative result) ×100%. The diagnostic coincidence rate = (the number of patients with true positive result + the number of patients with true negative result)/the total number of patients ×100%. Positive predictive value = the number of patients with true positive result/(the number of patients with true positive result + the

Basic data		
Age (Y)	≥27	37 (63.79)
	<27	21 (36.21)
Gestational week	≥30	40 (68.97)
	<30	18 (31.03)
Fertility	Primipara	33 (56.90)
	Multipara	25 (43.10)
History of fetus protection	Yes	10 (17.24)
	No	48 (82.76)
Family history	Yes	4 (6.90)
	No	54 (93.10)
Place of residence	Urban area	39 (67.24)
	Rural area	19 (32.76)
Smoking	Yes	8 (13.79)
	No	50 (86.21)
Drinking	Yes	11 (18.97)
	No	47 (81.03)

Table 1. Clinical data of the patients [n (%)

number of patients with false positive result) ×100%.

Outcome measures

All imaging results were reviewed by 3 senior chief physicians from the imaging department using a double-blind method. The prenatal ultrasonographic imaging features were analyzed, and the results of prenatal ultrasonography about each fetal urethral disease (hypospadias and posterior urethral valve) was compared with those of the individual pathological diagnosis. Additionally, the diagnostic value of prenatal ultrasonography was analyzed. Ultrasonographic imaging features of hypospadias: According to the two-dimensional ultrasonography, the penis was small and short and blunt at the end; the scrotum was separated like a "tulip"; the urine stream was fan-shaped instead of linear, or the urethra line had no continuity. According to the three-dimensional ultrasonography, the relationship between penis and scrotum was abnormal. Ultrasonographic imaging features of posterior urethral valve: According to the two-dimensional ultrasonography, there were bilateral hydronephrosis dilatation, cystauxe, bladder wall thickening, posterior urethral dilatation with "keyhole" sign, and amniotic fluid volume decrease. According to the three-dimensional ultrasonography, there was an obvious "keyhole" sign.

Statistical analyses

In this study, obtained data were analyzed statistically using SPSS 22.0 (Bomai Information Technology Co., Ltd., Guangzhou, China). Enumeration data were expressed as rate, and compared among multiple groups using the chisquare test. *P*<0.050 indicates a significant difference.

Results

Clinical data

The clinical data of all pregnant women including age, gestational age, fertility, history of fetus protection, family history, place of residence, smoking history, and drinking history are summarized in **Table 1**.

Imaging results

Ultrasonographic imaging features of hypospadias: In the diagnosis based on ultrasonographic imaging features, the occurrence rate of a small and short penis was found to be the highest, but the correct diagnostic rate of it was not found to be high, and the occurrence rate and detection rate of paruria and urethra continuity interruption were both found to be high, reaching 100.00%. In addition, in the diagnosis, the occurrence rate and correct diagnostic rate of transposition of the penis and scrotum were both found to be relatively low, and the occurrence rate and correct diagnostic rate of penis morphology abnormality and "tulip" sign were between those of the above three **Table 2**.

Ultrasonographic imaging features of posterior urethral valve: In the diagnosis based on ultrasonographic imaging features, the occurrence rate and correct diagnostic rate of cystauxe were both found to be the highest, while the occurrence rate of amniotic fluid volume decreased and the correct diagnostic rate of "keyhole" sign were found to be the lowest. In addition, in the diagnosis, the occurrence rate and correct diagnostic rate of bladder wall thickening and hydronephrosis were between those of the above three **Table 3**.

Diagnosis results

After natural delivery or induced delivery, among the 30 fetuses with suspected hypospa-

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Itom	Occurrence	Correct
	rate	diagnostic rate
Small and short penis	27 (90.00)	21 (77.78)
Penis morphology abnormality	22 (73.33)	16 (72.73)
"Tulip" sign	19 (63.33)	14 (73.68)
Transposition of the penis and scrotum	8 (26.67)	4 (50.00)
Paruria	7 (23.33)	7 (100.00)
Urethra continuity interruption	5 (16.67)	5 (100.00)

 Table 2. Ultrasonographic imaging feature analysis [n (%)]

 Table 3. Ultrasonographic imaging feature analysis [n (%)]

Item	Occurrence rate	Correct diagnostic rate
Cystauxe	28 (100.00)	26 (92.86)
Bladder wall thickening	26 (92.86)	23 (88.46)
"keyhole" sign	23 (82.14)	18 (78.26)
Hydronephrosis	25 (89.29)	21 (84.00)
Amniotic fluid volume decrease	6 (21.43)	5 (83.33)

Table 4. Ultrasonic diagnosis of hypospadias

	Pathological diagnosis (+)	Pathological diagnosis (-)	
Ultrasonic diagnosis (+)	17	2	19
Ultrasonic diagnosis (-)	9	2	11
	26	4	30

 Table 5. Ultrasonic diagnosis of posterior urethral valve

	Pathological	Pathological	
	diagnosis (+)	diagnosis (-)	
Ultrasonic diagnosis (+)	18	1	20
Ultrasonic diagnosis (-)	7	2	8
	25	3	28

dias, 26 fetuses were confirmed with hypospadias, and the other 4 fetuses included 1 fetus with normal male genitals, 1 fetus with concealed penis, and 2 fetuses with transposition of the penis and scrotum. A total of 19 fetuses were diagnosed with hypospadias according to ultrasonography, and the sensitivity of ultrasonography in diagnosing hypospadias was 73.08%. Among the 28 fetuses with suspected posterior urethral valve, 25 fetuses were confirmed with posterior urethral valve, and the other 3 fetuses included 2 fetuses with neurogenic bladder and 1 fetus with congenital megaureter. A total of 20 fetuses were diagnosed with posterior urethral valve according to ultrasonography, and the sensitivity of ultrasonography in diagnosing posterior urethral valve was 80.00%. **Tables 4** and **5**.

Evaluation of diagnostic efficiency

The sensitivities of ultrasonography in diagnosing hypospadias and posterior urethral valve were relatively high (65.38% and 72.00%), but the specificities in diagnosing hypospadias and posterior urethral valve were relatively low (50.00% and 66.67%). **Table 6**.

Discussion

As the destruction of the ecological environment and pollution of our water and food become more serious, fetal structural abnormalities are becoming increasingly com-

mon. For example, congenital heart defects are the most common congenital abnormalities in newborns, and its incidence is about 6-8 births per one thousand live births [15]. The causes of congenital malformations are complex. Environment and heredity are both influencing factors [16]. One study has reported that chromosomal aberration accounts for over 80% of the genetic causes of birth defects [17]. Birth defects have become the primary cause of death of newborns in the United States, accounting for approximate 20% of infant deaths [18]. Khokha MK et al. [19] have reported that about 8 million children are born with severe congenital defects each year, accounting for approximate 6% of the world's birth population. Congenital defects can also result in stillbirths and miscarriages, causing serious blows to families and society. Genitourinary system abnormalities, composed of abnormalities of the urethra, genitals, and scrotum, greatly harm children, which can give rise to the obstruction and dysfunction of the upper urinary tract and even the kidney [20]. At present, congenital urethral abnormalities, with a constantly increasing incidence, are the most common birth defects among newborns, and as such can result in serious adverse pregnancy outcomes and sexual dysfunction of the patients in their adulthood, that may need surgical intervention [21, 22]; so systematic prenatal examination is particularly important.

	Sensibility	Specificity	Diagnostic coincidence rate	Predictive positive value
Hypospadias	65.38	50.00	63.33	89.47
Posterior urethral valve	72.00	66.67	71.43	94.74

Table 6. Evaluation of ultrasonic diagnosis of hypospadias and posterior urethral valve (%)

It was found through clinical data of all participants in the study that the fetuses of pregnant women over 27 years were more prone to congenital urethral diseases. Cosme HW et al. [23] also believe that advanced age of pregnant women is related to congenital abnormalities of the fetus. The incidence of congenital urethral diseases among urban residents is higher than that among rural residents, and pregnant women with a relatively long gestational period, a history of fetus protection, smoking, and drinking have a relatively high incidence of diseases, which may be due to the fact that industrial pollution in urban areas is more serious and the coverage of prenatal examination in these areas is wider. Harmful substances contained in smoke easily affect the normal development of fetuses. One study by Harris BS et al. [24] has introduced in detail the close correlation of alcohol drinking, folic acid deficiency, and obesity with the increased risk of congenital abnormalities, and has also pointed out that drugs including retinoic acid and anticonvulsion drugs are closely related to various congenital defects. Hypospadias and posterior urethral valve are more common in congenital urethral diseases. Fetal hypospadias is caused by tubular disorder of the urethral wrinkled wall after the seventh week of embryogenesis, which can be classified into a balanus type, a penile type, a scrotum type, and a perineum type [25]. In this study, the small and short penis and "tulip" sign in the prenatal ultrasonographic imaging features are indirect signs of fetal hypospadias. Among hypospadias, the correct detection rate of paruria and urethra continuity interruption by ultrasonography was found to be the highest, reaching 100.00%. In addition, among the 30 patients with suspected hypospadias, 26 patients were confirmed with hypospadias through postpartum pathological examination, and 19 patients were confirmed through prenatal ultrasonography. The evaluation of diagnosis efficiency showed that although the specificity of ultrasonography in diagnosing hypospadias was not high (50.00%), its sensitivity and positive predictive value in diagnosing hypospadias were relatively high (65.38% and

89.47%, respectively). Posterior urethral valve is caused by the presence of a soft tissue membrane flap in the posterior urethra, which leads to urethral obstruction of different degrees. This study also analyzed the diagnostic value of prenatal ultrasonography for posterior urethral valve. The results showed that among the prenatal ultrasonographic imaging features of suspected patients, there were cystauxe, bladder wall thickening, and a "keyhole" sign, which may be due to the fact that urinary tract obstruction leads to bladder overfilling, thereby causing hydronephrosis of different degrees [26]. Among these ultrasonic imaging features, the occurrence rate and correct detection rate of cystauxe were both the highest, while the correct detection rate of a "keyhole" sign in posterior urethral valve was not high. By analyzing the diagnostic value, we found that the specificity of prenatal ultrasonography in diagnosing posterior urethral valve was also not high (only 66.67%), but its sensitivity and positive predictive in diagnosing the disease were both high.

In this study, 58 pregnant women whose fetus was suspected with congenital urethral diseases (hypospadias and posterior urethral valve) were enrolled as research subjects, and their ultrasonography results were analyzed. However, there are still some limitations in this study. For example, the size of the enrolled research subjects is small due to limited experimental conditions, and it cannot be excluded that different ultrasonic instruments may provide different imaging results. We will address these problems in future studies to obtain the most accurate results.

To sum up, prenatal ultrasonography has high sensitivity and positive predictive value in diagnosing hypospadias and posterior urethral valve, although its specificity is not high. Therefore, prenatal ultrasonography can be adopted as a reference for prenatal examination.

Disclosure of conflict of interest

None.

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