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Correlation of ureteric jet angle (UJA) with vesicoureteral reflux grade and its assessment as a noninvasive diagnostic parameter to detect vesicoureteral reflux

Poornima Maravi^{1*} , Lovely Kaushal¹, Bhagyashree Rathore² and Anshuli Trivedi³

Abstract

Background Vesicoureteral reflux (VUR) is an essential urogenital entity affecting infants and younger children. Many patients present late with recurrent urinary tract infections (UTIs), which lead to chronic pyelonephritis, renal scarring, and end-stage renal disease (ESRD). This progression in disease adds to significant morbidity and mortality in the paediatric age group. Voiding cystourethrography (VCUG) is the investigation of choice which is an invasive procedure and is related to the risk of ionizing radiation and iodinated contrast administration. Ureteric jet angle (UJA) is a Doppler parameter that can be obtained by measuring the angle between the horizontal axis of the floor of the optimally distended bladder and the Doppler ureteric jet at the ureteral opening into the bladder. The study aimed (1) to investigate the correlation of UJA with VUR grade and (2) to assess the utility of UJA as a noninvasive diagnostic indicator to diagnose VUR as an alternative to VCUG.

Method All paediatric patients with urinary complaints were evaluated by voiding cystourethrography (VCUG) for assessment of grades of VUR, followed by colour Doppler evaluation of ureteric jets. VCUG interpretations were made. UJA was calculated as the angle between the long axis of the colour Doppler jet and the horizontal axis of the floor of the optimally distended urinary bladder on colour Doppler examination. Ureteric jet angles were recorded on both sides irrespective of the presence of VUR, and data were analysed using SPSS. The correlation coefficient (r) with p value was calculated. The diagnostic efficacy of UJA (58° or more) to detect VUR was assessed by calculating sensitivity, specificity, PPV, NPV, positive LR and negative LR. The AUC was calculated to evaluate the diagnostic efficacy of UJA 58° or more to detect VUR.

Results In total, 34 (68 renal units) children (8 months–12 years), including 20 males (M) and 14 females (F), examined. The mean age was 4.96 ± 2.87 years for the total population, including 4.60 ± 2.02 years for boys and 5.47 ± 2.75 years for girls. Twenty-one patients (10 girls and 11 boys) showed VUR on MCUG. Eight patients showed high grades (grade III–V), including seven boys and a girl. The range of UJA in VUR-negative patients was $27\text{--}60^\circ$ with a median angle of 42.03° . VUR-positive patients showed an angle range of $32\text{--}71^\circ$ with a median angle of 62.13° . High-grade VUR was seen in 8 patients with an angle range of $59\text{--}84^\circ$ and a median angle of 76.31° . A positive correlation ($r=0.81$) was noted between UJA and VUR grading. The sensitivity and specificity of angle $> 58^\circ$ to detect VUR were 0.66 and 0.92 with PPV 0.93 and NPV 0.63. Yuden's J value was 58° . The value for the area under the curve was 0.7.

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Conclusions Positive linear correlation was seen between UJA and VUR grades with high specificity and positive predictive value. The Diagnostic Utility of UJA 58° as a screening method to detect severe VUR was acceptable and can be further studied with a larger sample size.

Keywords Doppler, Ureteric jet angle, Vesicoureteral reflux, Area under curve

Background

Vesicoureteral reflux (VUR) is the most common congenital urinary tract in children associated with the abnormal development of the UVJ. VUR is a critical risk factor for developing urinary tract infections in the paediatric population [1]. It is observed in ~30% of children presenting with urinary tract infections and about ~1% of the general population [2–4].

Untreated VUR leads to parenchymal injury and fibrotic scarring of the kidney, known as reflux nephropathy (RN), which is a significant cause of end-stage renal disease (ESRD) [5]. Chronic renal failure in these patients requires long-term dialysis and renal transplantation [6, 7].

Micturating cystourethrogram (MCUG) is the method of choice to diagnose VUR in children, which involves urinary catheterization and administration of a contrast agent into the bladder [8]. The risk of exposure to ionizing radiation is involved. Moreover, MCUG has a low detection rate to diagnose early and mild (low-grade) VUR. On that account, noninvasive, contrast free and radiation-free methods are required to diagnose VUR.

Only a few studies have demonstrated the utility of ureteric jet angle (UJA) and its significance in diagnosing VUR [9]. In this study, we attempt to correlate the UJA with grades (severity) of VUR and evaluate its role as an indicator to diagnose VUR in children. Early diagnosis/screening of children with this parameter can provide prophylactic antibiotic coverage to prevent secondary urinary tract infection (UTI), reducing morbidity and mortality in these patients.

Methods

In this hospital-based, cross-sectional study, we evaluated 34 children (total 68 renal units) of age group 8 months–12 years with urinary symptoms referred to the Department of Radiodiagnosis, GMC, Bhopal, for VCUG from January to June 2020 following the approval from institutional ethical committee. The patients were divided into VUR positive (cases) and VUR negative (controls) groups according to the presence of VUR in VCUG, and individual grades of VUR were noted according to the international grading system of VUR.

VCUG is the standard gold method to confirm the presence of VUR in infants and children. It also provides

a detailed anatomy of the bladder and urethra. For performing VCUG, first informed written consent was obtained from parents, and the procedure was explained. All patients came with a urinary catheter in place from referring clinical departments. The empty bladder was gradually distended with a mixture of normal saline (20%) and radio-opaque contrast media Omnipaque (Iohexol 350 mg I/ml, 80%) under fluoroscopic guidance. After achieving optimal distension (observer-dependent), full bladder, micturating, and empty bladder, spot films were taken. Interpretations were made, and documentation was done.

For UJA measurements, all patients, irrespective of the presence of VUR on VCUG, were evaluated by the 2D (Figs. 1, 2, 3 4 and 5) and colour Doppler sonography (Fig. 6). Patients were examined in the supine position for about 10–15 min with BPL E-CUBE B, 2D, and a colour Doppler machine following the adjustments of appropriate USG parameters. Though the ultrasound

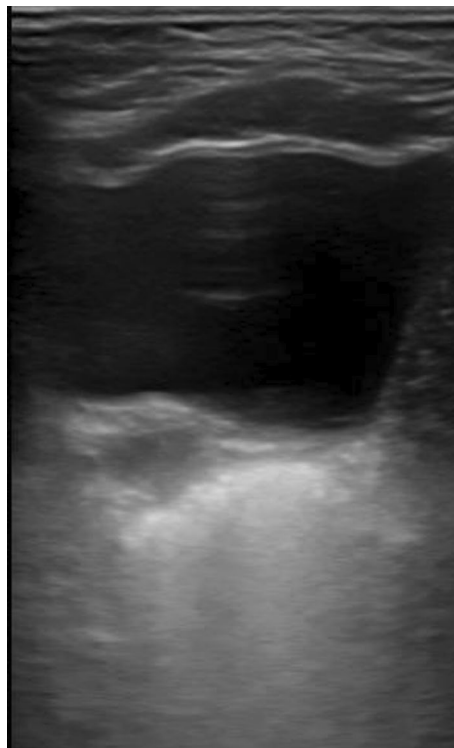


Fig. 1 Distended Urinary bladder in transverse axis

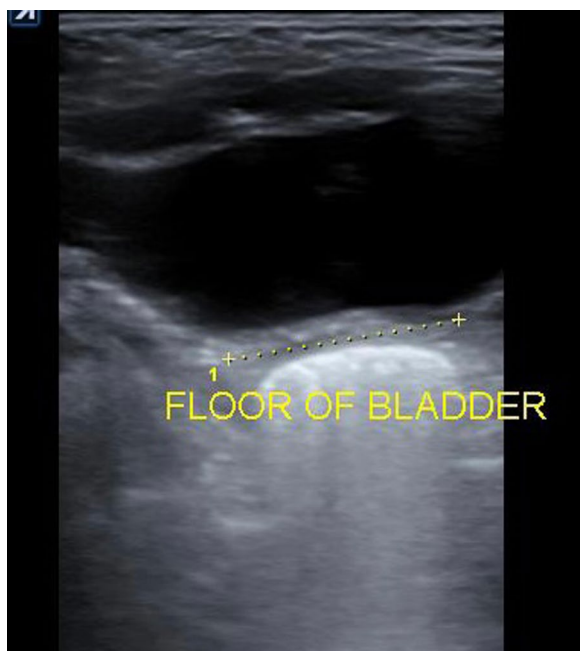


Fig. 2 Depiction of the horizontal floor of the distended urinary bladder

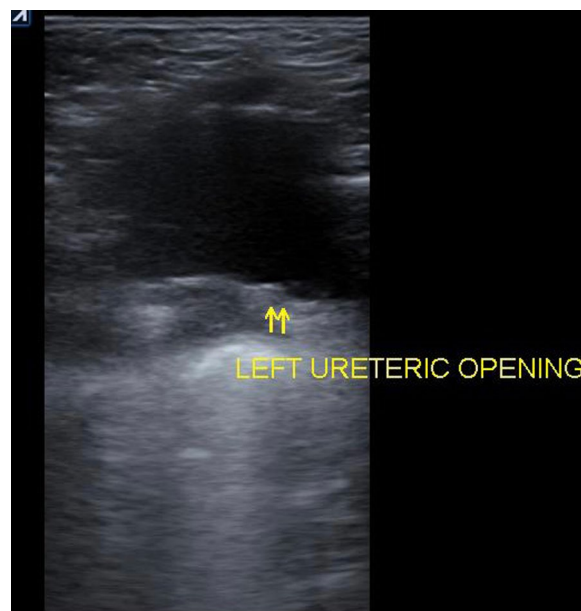


Fig. 4 Visualization of left ureteric orifice



Fig. 3 Visualization of the right ureteric orifice

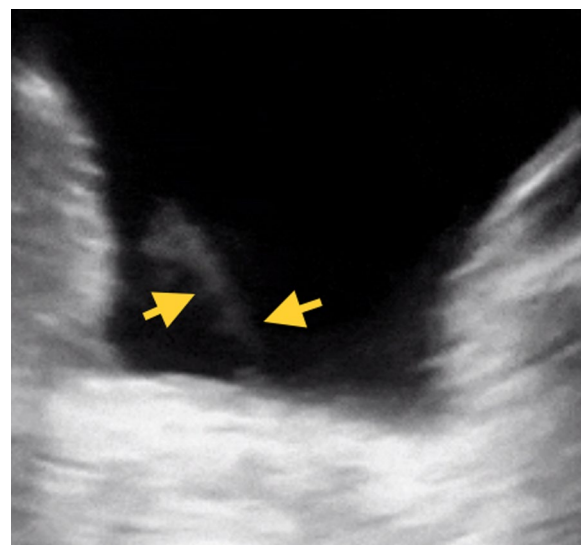


Fig. 5 Grey scale depiction of ureteric jet angles as moving echoes

parameters varied for each patient, the frequency was 6.0 on 2D and 6.5 on colour flow images in most patients (age group 8 months–3 years). The other parameters were as follows-

For 2D-Frq=6.5, $P=100\%$, Gn=49, DR=77, FR=15, $D=7.0$ and colour flow (CF)—Frq=6.0, $p=100\%$, Gn=50, WF=4, with 0.9 kHz. Due to difficulty localizing bilateral ureteric jets in a single transverse plane, each side was examined as one after another. Angles on both

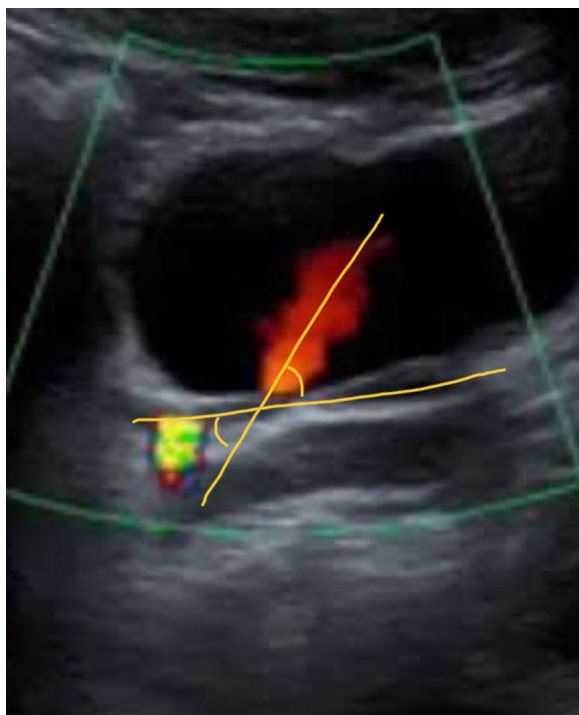


Fig. 6 Schematic diagram to visualize and calculate ureteric jet angle on colour Doppler ultrasonography

sides were recorded. The ureteric jet was identified as fast-moving echoes from the ureteric orifice with linear colour coding on each side (Figs. 5 and 6). Images were frozen, and the auto-calculated angle with three points between the longitudinal axis of this linear colour coding and the horizontal floor of the optimally distended urinary bladder (Fig. 2) was measured on a transverse scan with a high-frequency linear probe (5–7.5 MHz). Most infants and younger children were examined during sleep. No sedation was given.

Statistical analysis

We analysed the data using the updated version of SPSS. Quantitative variables were described as median values. For the assessment of categorical variables, the Pearson chi-square test was utilized. The correlation coefficient (r) was calculated, and for the signification of any correlations between variables, the p value was derived with a significance level of less than 0.05. The confidence interval was 95%. The cut-off angle of 58° was calculated from Youden's J index. The diagnostic efficacy of UJA 58° or more in detecting VUR grade was calculated, including sensitivity, specificity, PPV, NPV, and likelihood ratios using standard formulas (using the number of true positives, true negatives, false positives and false negatives). In addition, AUC was calculated to assess the diagnostic efficacy of (UJA 58° or more) to detect VUR.

Table 1 Age-wise distribution of angle range and median angle

Age	Angle range	Median angle
8 months–3 year	40–84	58.28
VUR positive	40–84	64
VUR negative	40–60	48
4–6 years	27–84	53.55
VUR positive	45–84	62
VUR negative	23–46	33.83
7–9 years	45–76	59.37
VUR positive	46–76	63
VUR negative	27–49	39
10–12 years	27–73	44
VUR positive	44–45	44.5
VUR negative	–	–

All angles are in degree

Results

A total of 34 children (Total of 68 renal units), including 20 males (M) and 14 females (F), were examined. The overall incidence of VUR was 0.61 in VCUG. Age ranges from 8 months (0.66 years) to 12 years. The mean age was 4.96 ± 2.87 years for the total population, including 4.60 ± 2.02 years for boys and 5.47 ± 2.75 years for girls. The total population angle ranges from 27 to 84° with a median angle of 54.5° . Out of 34 children, 21 (61.74%) patients showed evidence of VUR, including 11 (55.00%) males and 10 (71.42%) females (Table 1). 13 children showed normal findings on VCUG (Table 1). Significant overlapping of UJA was seen when groups were compared between VUR positive and VUR negative populations; however, statistically, significantly higher angles were seen in the VUR positive population ($p < 0.005$).

In the VCUG-positive population (for VUR), the angle ranges from 40 to 84° with a median angle of 62.13° . On the other hand, the negative population angle ranges from 27 to 60° with a median angle of 42.03° .

Under the age group 8 months–3 years, 14 (41.71%) patients were examined, including nine males and five females. Under this age group, the VUR positive population angle ranges from 40 to 84° with a median angle of 64° , and VUR negative population angle ranges from 40 to 60° with a median angle of 48° . Under the age group 4–6 years, ten patients (29.41%), including seven males and three females, were evaluated. In VUR-positive cases, the angle varies from 45 to 84° with a median angle 62° . In VUR negative cases, the angle ranges from 23 to 46° with a median angle 33.8. In the age group 8 months–3 years, mean ureteric jet angles were higher with increased refluxing units. A total of 16 cases showed bilateral refluxing units. Under the age group of 7–9 years (all female children), the VUR-positive population (total

of four patients) showed an angle range from 46–76° with a median angle of 63° (11.76%). In VUR negative population under this age group angle ranges from 27 to 49° with a median angle of 39°. Under the age group of 10–12 years, 6 (17.64%) children showed VUR in VCUG with UJA ranging from 44–45°, with a median angle was 44.5°. In VUR negative population under this age, the group angle ranges from 27 to 45° with a median angle of 39° (Table 1).

In male children, 11 (32.35%) males show VUR in MCUG with an angle range of 44–84° and a median angle of 65.59°. On the other hand, VUR hostile male population shows a rise ranging from 23 to 60° and a median angle of 44.27°. Ten (29.41%) female children show some evidence of VUR on MCUG with an angle range of 42–79° and a median angle of 58.5°. On the other hand, the negative female population offers an angle range from 27 to 53° with a median gradient of 37°.

Overall median angles were higher in the male population than in the female population. The median angle was also higher in VUR positive male population compared to VUR negative male population.

In VUR positive male population, the median angle was large (69.11°), and the VUR grade was high when similar findings were compared to the female population. Positive female children show a median angle of 62.66° with a milder VUR grade (I). Male children with bilateral refluxing units also showed significantly high VUR grades (Tables 2 and 3).

The male population shows high incidences of VUR with higher grades (median grade III, seen in 5 male children) with a median angle of 69.84°. On the contrary, the female child population show low grades (most

frequently grade I). In refluxing units, higher rates were seen in only two female children, with a mean angle of 54.35°.

A total of 8 children show High grade (III–V) VUR and a median angle of 76.31°. Thirteen children show low-grade VUR (I–II) with a median angle of 54.23°.

Widespread occurrence and grade of VUR were higher in bilateral ureters, i.e., 15 (71.42% {9 M+6F}), eight patients from the age of 8 months–6 years showing high grade (III–IV) VUR, five children under the age of 8 mon-3 years showed the equal number of cases. Isolated right (3) and left side VUR (3), and both sides were showing female predominance (2 females out of 3). The average angle in bilateral refluxing units was 68.2 on the right (R) and 64.8 on the left (L), which were higher on the right side. Grade I VUR was seen most frequently in bilateral refluxing units. Grade I VUR was also seen most frequently in children aged 1–10 years (total of 4). No sex predilection was seen in isolated right-sided VUR. In right-sided, isolated refluxing units, the angle ranges from 45 to 65° with a median angle of 48°. In left-sided isolated refluxing units, the grade ranges from 44 to 63 with a median angle of 63° (Tables 3 and 4).

Nine male children, with a mean age of 2.91 year, showed sonographic features of urinary tract infection/cystitis in contradictory to only one 9 year, old female.

A positive linear correlation between UJA and grades of VUR is seen with a significant *p* value (*p* < 0.05) for grades of VUR (Table 5).

Cut off the angle of 58° or less was calculated from Youden’s J index. The overall sensitivity of curve 58° or more to detect VUR was 0.66, which means the probability of getting VUR in children with urinary complaints is low. Therefore, it has a low potential for recognizing children with VUR. On the other hand,

Table 2 Laterality wise distribution of VUR

Age	Right sided VUR	Left Sided VUR	Bilateral VUR
8 months–3 years	7	4	7
4–6 years	4	2	6
7–9 years	1	2	5
10–12 years	1	1	3
Total	13	9	21

Table 4 Gender-wise distribution of refluxing units with mean age and grades

Refluxing units	Males	Females	Mean age (In years)	Grades (Of VUR)
16	7	1	2.87	High (III/V)
20	4	9	5.46	Low (I/II)
Total	11	10		

Table 3 Gender-wise distribution of angle range and grades in refluxing and nonrefluxing units

Mean age	Male	Female	VUR	Grade	Angle range	Mean angle	Total
2.91 Y	7	2	+	4	48–84	72.05	9
9 Y	0	1	–	–	45–53	49	1

All angles are in degree

Table 5 Values of correlation coefficient and p value in refluxing units with grades of VUR and median angles

Refluxing units	Grades	Angle range (in degree)	Median angle (in degree)	Correlation coefficient (r)	p value (<0.05 is significant)
16	High (III/IV)	59–84	76.31	0.470	0.005*
20	Low (I/II)	40–76	54.23	0.530	0.001*

*p value (<0.05 is significant)

Table 6 Diagnostic accuracy of angle 58° or more for detecting VUR grades

Diagnostic efficacy of angle 58° or more	Value	Interpretation
Sensitivity	0.66	Low
Specificity	0.92	High
PPV	0.93	High
NPV	0.63	Low
PLR*	+0.36	Low
NLR**	−8.25	High
AUC	0.7	Acceptable

*Positive predictive ratio

**Negative predictive ratio

the overall specificity of an angle 58° or more to detect VUR is 0.92, which means the probability of getting negative VUR in healthy children is high. However, sensitivity and specificity vary greatly depending on the spectrum of VUR in the studied population (Table 6).

The positive and negative predictive values for this parameter (UJA) to diagnose high-grade VUR were 0.93 and 0.63, respectively. The probability of having the VUR in VUR-positive children is high (PPV = 0.93). However, the likelihood of not having VUR in VUR-negative children is low (NPV = 0.63). The likelihood ratio for diagnosing negative cases was 0.36 and for positive patients was 8.25. The high positive likelihood ratio suggests angle >58° is more indicative of VUR. These ratios explain how much more likely positive test results occur in children with VUR than those without VUR. The negative likelihood ratio (LR-) for angle 58° to detect VUR is 0.36 for this study, which suggests this parameter may prove to be of value for ruling out the diagnosis (Table 6).

The area under the curve (AUC) was 0.7, which suggests the acceptability of this parameter as a screening tool to detect high-grade VUR.

Discussion

Hiroshi et al. [9] were the first (in 2016) to evaluate the role of UJA in detecting VUR in children. In their study, they evaluated children with urinary tract infections or hydronephrosis. They concluded that mean ureteric jet angles were significantly higher in refluxing units (67.9°) than in non-refluxing units (47.8°). Similar findings of higher angles in refluxing units (60.47°) and lower in non-refluxing units (42.59°) were reported by Nedra et al. [10]. Both studies have also suggested a greater angle for each reflux grade. In our research, we have evaluated symptomatic children with urinary complaints irrespective of the presence of urinary tract infection, hydronephrosis, or other detectable urinary abnormalities with a higher median angle in refluxing units (62.13°) and lower angles in non-refluxing units (42.03°) similar to above two studies with positive linear correlation ($r=0.81$) between UJA and reflux grade suggesting high grade for higher angles.

There were many refluxing units in the age group 8 months–3 years compared to the age group 10–12 years 1. This difference suggests that the incidence of VUR is higher in infants and younger children than the older children. These results support previous literature, offering increased incidences of VUR in infants more than in younger children [3]. Longitudinal studies have demonstrated that ~50 to 65% of cases of non-syndromic primary VUR undergo spontaneous resolution with age [11, 12]. The mechanism leading to this resolution is not studied; however, the elongation of the intra-vesical ureter (0.5 cm at birth vs 1.5–2.5 cm in adults) due to somatic growth has been suggested as an explanation for the improved function of the VUJ in older children [13]. Alternatively, morphological changes in the bladder and ureter's smooth muscle layer and its supporting extracellular microenvironment could be why most VUR resolves over time [14, 15]. High-grade VUR was also reported in children younger children <1 year, and low-grade VUR were mostly seen in older children between ages 3–5 year by Lipana et al. [16]. Still, no statistical difference was noted in their study's proportion of patients having VUR by age group.

In addition, high-grade VUR causes repeated urinary tract infections leading to significant renal damage in infants [16]. Studies have shown that in children under the age of 1 year with a urinary tract infection, 70% will have VUR. This number decreases to 15% by the age of 12. The younger the patient and the lower the grade at a presentation, the higher the chance of spontaneous resolution. Approximately 85% of stage I & II VUR cases will resolve spontaneously. About 50% of grade III VUR and a lower percentage of higher grades will also resolve spontaneously.

In this study, the overall incidence of VUR was higher (71.42%) in the female population, however, low-grade, compared to the male children [17, 18]. Some studies showed that VUR is more common in males antenatally; however, there is a definite female preponderance in later life, with 85% of cases being female. Hiraoka et al. [12] found no gender difference in the incidence of VUR detected in the prospective study of babies from mothers with a positive family history of VUR. Most of the VUR identified in family studies were classified as low grades without dilation of the renal pelvis or ureter [19, 20].

In this study, the male population showed higher grade VUR (7 males with 63.63%) in contradiction to the female population (10%, 8 months old female infants). This finding supports other studies showing that most VUR in male infants is of higher grades, whereas VUR in female infants is equally distributed between low and high grades [9]. Lipana et al. [16] reported similar results, with more males having higher VUR grades in both the right and left kidneys than females. Still, there was no statistical difference in the proportion of patients with VUR according to sex. The primary reason is frequent voiding dysfunction/ high urethral resistance found in male babies, which enhances intra-vesicle pressure and causes higher VUR incidences in male infants [13, 14]. However, this finding also allows for earlier detection of VUR by ultrasound in male infants (by causing repeated urinary symptoms).

Average angles were higher (63°) on the left side when compared to right refluxing units (48.33°), which is in support of previous studies which showed high angles on the left side [11].

Additionally, Asanuma et al. [9] evaluated the diagnostic accuracy of cut-off UJA 70° or more to detect grade IV/V VUR with a sensitivity of 0.81 and specificity of 0.82, which were higher than our study. However, results similar to our research (diagnostic efficacy of cut-off angle 58° with relatively lower sensitivity 0.66 and higher specificity 0.92) have also been reported by Zadeh et al. [10], who has evaluated the diagnostic efficacy of cut-off angle 50° with sensitivity and specificity of 0.70 and 0.79, respectively.

In our study, the value for the area under the curve was 0.7, less than the diagnostic efficacy reported by Hiroshi et al. [1] but similar to the effectiveness written by Lipana et al. [16].

Lipana et al. [16] also stated low sensitivity and negative predictive value of angle 52 to detect high-grade VUR with AUC < 0.7. They evaluated the sensitivity and specificity of curve 52° to detect VUR, which were 0.60 and 0.58, with poor correlation between ureteral jet angle and VUR owing to functional abnormalities such as voiding dysfunction in examined population [12]. Though not

promising, this value suggests the acceptability of this parameter (UJA) as an alternative tool to diagnose high-grade VUR in children.

The significant difference between the diagnostic efficacy of this parameter (UJA) from other studies can be due to the small sample size of the population in the present study.

Mohanan et al. [21] have reported that higher grade VUR (IV/V) is related to moderate to severe renal scarring. However, the prevalence of this renal dysfunction was found to be lower in children with high-grade VUR without the occurrence of urinary tract infections (UTI). This suggests early detection by screening (by measuring UJA in these children) can prevent urinary tract infections (by administering prophylactic antibiotics) and could avoid ESRD.

Therefore, early diagnosis in children is crucial as studies have shown that the children with VUR who present with a UTI and associated acute pyelonephritis are more likely to develop permanent renal cortical scarring than those without VUR, with an odds ratio of 2.8. Thus VUR increases the frequency of UTIs and the risk of damage to upper urinary structures and end-stage renal disease [6].

The limitation of the study

Low sensitivity of UJA equal or > 58° to detect VUR in this study may be attributed to the smaller sample size and widely varying spectrum of VUR in the studied population. Furthermore, the interpretations and values may not be precise. Therefore, these results cannot be generalized in an entire paediatric population, and firm conclusions about the positive outcomes cannot be made.

Conclusions

Measuring ureteric jet angle on colour Doppler is a simple, easy, and acceptable technique for detecting VUR in children. Furthermore, this parameter is noninvasive and does not involve any contrast administration. So this novel parameter can be used as an alternative to VCUG to diagnose high-grade VUR; however, more research with a larger sample size is suggested.

Abbreviations

VUR	Vesicoureteric reflux
VCUG	Voiding cystourethrogram
UJA	Ureteric jet angle
R	Right
L	Left
M	Male
F	Female
ESRD	End stage renal disease
PPV	Positive predictive value
NPV	Negative predictive value
LR	Likelihood ratio

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Author contributions

PM was involved in design of work, interpretation of data, drafting of work, revision of work. LK contributed to design of creation. BR was involved in data acquisition. AT contributed to analysis of data. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets generated and analysed during this study are not publicly available due to the restricted data sharing policy of the institute but are available from the corresponding author upon reasonable request.

Declarations**Ethics approval and consent to participate**

Written informed consent obtained. Ethical committee of Gandhi medical college and Hamidia Hospital, Bhopal, Madhya Pradesh, India.

Consent for publication

Written consent obtained.

Competing interests

The authors declare that they have no competing interests.

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