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Preoperative evaluation of the persistent urogenital sinus in cases with congenital adrenal hyperplasia

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Abstract

Background Congenital adrenal hyperplasia (CAH) is a common cause of urogenital sinus (UGS) anomalies. Delineating the abnormal anatomy of the UGS is crucial prior to the operative repair. Genitography and cystourethroscopy are commonly used by most surgeons to plan for reconstruction. We aim at this study to evaluate the role of these modalities and to compare their accuracy in delineating the abnormal anatomy.

Methods We did a prospective study of 30 female paediatric patients with persistent UGS secondary to CAH. All cases were evaluated with genitography and cystourethroscopy. We compared the accuracy of each modality in delineating the confluence. The confluence depth, the urethral length proximal to the confluence, the vaginal dimensions, and the depth of the bladder neck were measured in the genitograms.

Results Cystourethroscopy showed the abnormal anatomy in all 30 cases (100%). The genitogram showed the site of confluence in 24 cases out of 30 cases (80%). According to the site of the vaginal opening in relation to the external urethral sphincter in the genitogram, we had 2 groups: the low confluence group ($N=14$) and the high confluence group ($N=16$). The mean confluence depth in the low group was 9.8 mm vs. 20.5 mm in the high group (p-value <0.001). To find a cutoff point to differentiate low from high groups, we used the values that resulted from dividing the length of the urethra proximal to the confluence over the depth of the bladder neck. By using the ROC curve, the cutoff point was 0.63 mm (< 0.63 mm high, > / = 0.63 mm low) (p-value $<.001$).

Conclusion We recommend using both cystourethroscopy and genitography for preoperative evaluation. Cystourethroscopy is superior in identifying the abnormal anatomy, but it lacks precision in taking measurements. Genitography can avoid this drawback and can precisely measure the confluence depth, vaginal dimensions, and length of the proximal urethra. We suggest using this formula (length of the urethra proximal to the confluence/depth of bladder neck) to classify persistent UGS as low (> / = 0.63 mm) and high (< 0.63 mm).

Keywords Persistent urogenital sinus, Congenital adrenal hyperplasia, Genitogram, Cystourethroscopy

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Background

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder characterised by impaired cortisol synthesis. The worldwide incidence in most studies ranges from1:14,000 to 1:18,000 births [1]. A cardinal feature of CAH in newborn females is the abnormal development of the external genitalia with variable extent of virilisation and persistent urogenital sinus (UGS). In persistent UGS, the urethra and vagina form a common channel (urogenital sinus) with a single external opening [2].

The radiological assessment of persistent UGS is crucial for surgical planning. Imaging studies are essentially based on ultrasonography, contrast studies, endoscopy, and magnetic resonance imaging (MRI) [3]. The genitogram demonstrates a male or female-type urethral configuration, the communication with the vagina and cervical impression [4]. One of the most helpful diagnostic studies for defining the anatomy for surgical reconstruction is endoscopy. In patients with CAH, cystourethroscopy is usually performed at the time of surgery but may be necessary as a separate early procedure to help with gender identity in other disorders of sexual development (DSD) cases or if the vagina is not identified in genitography [5].

Most classify CAH as low or high, but there is no consensus about the definition of high or low UGS. Some descriptions have noted the vagina as being 'high' if thought to enter above the external sphincter [6, 7]. Some use the length of the common channel; if it is more than 2.5 cm [8] or 3 cm [9, 10], it is considered high UGS. Recently, measuring the length of the urethra proximal to the confluence has been recommended instead (high if less than 1.5 cm) [11, 12]. Some depends on referring the level of lower end of the vagina (urogenital confluence) to a fixed bony landmark, 'the pubic symphysis' in the MRI to diagnose high UGS. They diagnose high UGS when the vagina terminates almost at the distal end of the pubic symphysis or above [13]. In the present study, we compared the accuracy of genitography versus cystourethroscopy in correctly delineating the abnormal anatomy in cases with persistent UGS secondary to CAH.

Methods

This was a prospective cohort study, including all female patients presenting to the Paediatric Surgery Department, Cairo University Egypt, with persistent urogenital sinus secondary to CAH, in the period between May 2021 and February 2023.

All patients with persistent urogenital sinus had a contrast genitogram performed using Omnipaque® under fluoroscopy guidance, the same technique used in our centre in a previous study [14]. We used the measurements that were described and illustrated in other studies [14–16]. Patients were generally anesthetised either in the same setting of surgery or preoperatively in a different setting. A radio-opaque marker of known dimensions was placed at the perineum about 2–2.5 cm anterior to the limit of the anal verge. The positioning of the patient was done in an exact lateral position while putting both femurs precisely aligned together and pulling both thighs towards the patient's abdomen. A 6F catheter was inserted into the external opening for just 1 cm.

Contrast material was injected under fluoroscopic guidance with moderate pressure until the confluence was delineated. If difficulty appeared in introducing contrast to the vagina, the catheter was manipulated by pushing, pulling, and rotation with an injection under a higher pressure by closing the external opening with the thumb and index finger to avoid leakage. The depth of confluence from the perineal marker was measured in ratio to the perineal marker dimensions, whatever the scale of the genitographic picture was, and measurements were taken in millimetres. Other measurements of the urethra proximal to the confluence, the vaginal dimensions, and the depth of the bladder neck were taken (Fig. 1).

All cases were further investigated using rigid 9.5F cystoscopy with a thirty-degree lens. The scope was introduced along the UGS and advanced into the bladder. Most of the times, it finds its way easily to the bladder

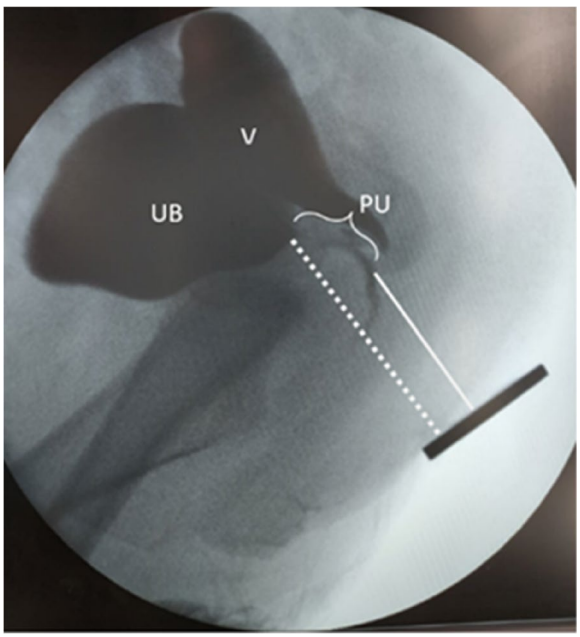

Fig. 1 Genitography measurements. UB, urinary bladder; V, vagina; PU, urethral proximal to the confluence; solid line, confluence depth; dotted line, bladder neck depth

more than the vagina due to the narrow vaginal orifice and posterior location which make it better searched for in a retrograde pattern with high saline flow.

In cases where the genitography failed to show the vagina, we performed a cystourethroscopy and inserted a catheter inside the vagina, then we injected the contrast through it to evaluate the vaginal dimensions, the confluence depth, and the length of the proximal urethra preoperatively.

We adopted the classification that describes a high UGS if the vaginal opening is above the external sphincter. As all our patients were virilized, the urethral anatomy is more similar in appearance to a male than a female urethra. When the urethra is inserted into the perineum, it resembles a bulbar urethra that bends and goes deeply inward towards the bifurcation of the corpora cavernosa. Therefore, above this bend is the external urethral sphincter. So, if the vagina in the genitogram enters the UGS above this level, it is a high UGS, and below, it is a low UGS (Figs. 2 and 3).

Data were coded and entered using the statistical package for the Social Sciences (SPSS) version 28 (IBM Corp., Armonk, NY, USA). Data was summarised using mean and standard deviation for normally distributed quantitative variables or median and interquartile range for non-normally distributed quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired *t*-test in normally distributed quantitative variables, while non-parametric Mann–Whitney test was used for non-normally distributed quantitative variables. Comparison between the length of the urethra proximal to the confluence and the expected urethral length for age in each type was done using paired *t*-test (Chan, 2003a). Correlations between quantitative variables were done using Spearman correlation coefficient (Chan, 2003b). ROC curve was constructed with area under curve analysis performed to detect the best cutoff value of significant parameters for detection of high type. *P*-values less than 0.05 were considered statistically significant.

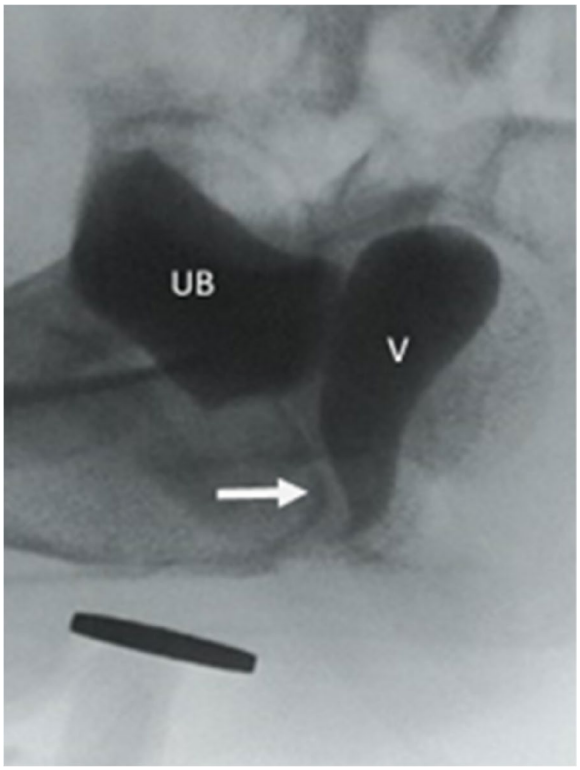

Fig. 2 Genitogram showing a low persistent urogenital sinus where the vaginal opening is below the urethral bend (arrow). UB, urinary bladder; V, vagina

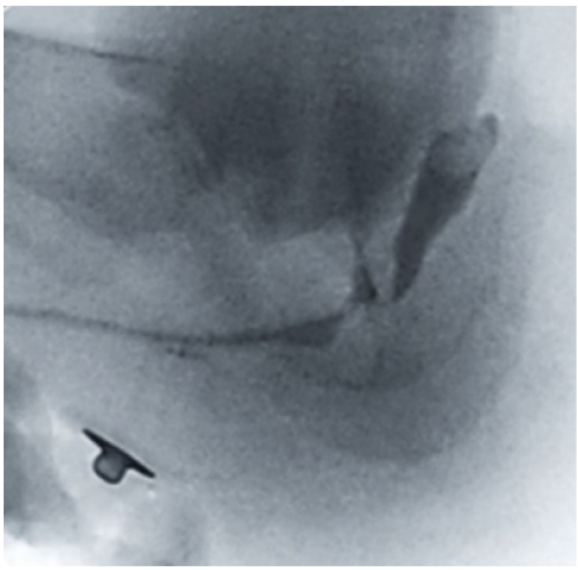

Fig. 3 Genitogram showing a high persistent urogenital sinus

Results

Thirty cases were included in this study. All cases had persistent urogenital sinus secondary to congenital adrenal hyperplasia. The median age was 36 (9–109) months. All cases were investigated with a cystourethroscopy and a genitogram. Cystourethroscopy showed the abnormal anatomy in all 30 cases (100%). The genitogram showed the site of confluence in 24 cases out of 30 cases (80%). In the remaining 6 cases, cystourethroscopy was used to catheterise the vagina and inject the contrast so the site of the confluence could be delineated. The depth of the bladder neck from the perineum and the confluence depth were measured in the genitograms. There was no

correlation between age and the depth of the bladder neck or the confluence depth.

According to the site of the vaginal opening in relation to the external urethral sphincter in genitogram, we had two groups: the low confluence group ($N=14$) and the high confluence group ($N=16$). The genitogram measurements are shown in Table 1.

The estimated normal urethral length for the corresponding age group was calculated using this formula: urethral length in mm = 0.0919 × age in months + 15.752 [17].

We compared it to the length of the urethra proximal to the confluence in the two groups. In the low group, the mean length of the urethra proximal to the confluence was longer than the mean of the estimated normal urethral length for the corresponding age 23.9 mm vs. 20.5 mm (p-value 0.035). In the high group, the mean length of the urethra proximal to the confluence was shorter than the median of the estimated normal urethral length for the corresponding age 15 mm vs. 19.49 mm (p-value 0.003). To find a cutoff point to differentiate low from high groups, we used the values that resulted from dividing the length of the urethra proximal to the confluence over the depth of the bladder neck. By using the ROC curve, the cutoff point was 0.63 mm (< 0.63 mm high, > / = 0.63 mm low) (p-value < 0.001). At this cutoff point, the sensitivity and specificity were 100% and 100%, respectively.

Discussion

The radiological assessment of persistent UGS is of the utmost importance before any attempt at reconstructive surgery for this challenging condition [14]. We chose to study the genitography and the cystourethroscopy in the preoperative evaluation of CAH cases with persistent UGS because they are widely used. We believe that MRI can give us valuable information, but it is not a substitute for genitography and cystoscopy. As its interpretation needs experience and it will not give us an accurate vaginal dimension if it is not distended with fluid.

In this study, cystourethroscopy showed the abnormal anatomy in 100% of the cases, and the genitogram showed the site of confluence in 80% of the cases, which supports the findings of other studies [14, 18, 19]. VanderBrink et al. retrospectively reviewed the records of 40 patients with congenital adrenal hyperplasia who underwent feminising genioplasty, and they correlated the preoperative genitogram findings with cystoscopic and operative findings. They found that genitography did not completely reveal urogenital sinus anatomy in 25% of patients who underwent the examination [18]. Ashour et al. did a prospective cohort study, including 12 patients presenting with a persistent urogenital sinus secondary to CAH. They compared the accuracy of the contrast radiographic studies versus diagnostic cystourethroscopy. They found that preoperative contrast radiography was accurate only in 83% of cases, whereas cystourethroscopy was accurate in 100%, and concluded that cystourethroscopy is superior to conventional contrast studies in demonstrating the abnormal anatomy [19]. Although cystoscopy delineated the anatomy in 100% of the cases, we could not rely only on it, as taking measurements using cystoscopy has a lot of fallacies, especially when we are talking about millimetres. Also, cystourethroscopy could measure the length of the confluence, not the depth. In fact, the length of the sinus may be irrelevant since much of its course is in the perineum, parallel to the surface. More important to predict the ease or complexity of the surgery is the distance from the confluence of the vagina and urethra to the perineal skin (depth) and the length of the urethra proximal to the confluence. To include these parameters, we suggested using this formula (length of the urethra proximal to the confluence/depth of bladder neck) to classify persistent UGS as low and high. We found the cutoff point to be 0.63 mm (< 0.63 mm high, > / = 0.63 mm low). This would help to classify cases of persistent UGS without external virilisation.

Conclusion

In this study, we recommend using both cystourethroscopy and genitography for preoperative evaluation. Cystourethroscopy is superior in identifying the abnormal anatomy. Also, it can be used to catheterise the urethra and the vagina and to inject contrast into the vagina when it is not visualised in genitography. But it lacks

Table 1 The genitogram measurements in the two groups

Genitogram measurements in mm	Types of urogenital sinus				*P*-value
	Low confluence group ($N=14$)		High confluence group ($N=16$)		
	Mean	Standard deviation	Mean	Standard deviation	
Confluence depth in mm	9.80	2.74	20.50	6.24	**< 0.001**
Length of proximal urethra in mm	23.90	4.48	15.00	3.70	**< 0.001**
Depth of bladder neck in mm	33.70	6.15	35.50	5.27	0.450

precision in taking measurements. Genitography can avoid this drawback and can precisely measure the confluence depth, vaginal dimensions, and length of the proximal urethra. We suggest using this formula (length of the urethra proximal to the confluence/depth of the bladder neck) to classify persistent UGS as low (> / = 0.63 mm) and high (< 0.63 mm).

Abbreviations

CAH	Congenital adrenal hyperplasia
UGS	Urogenital sinus
MRI	Magnetic resonance imaging
DSD	Disorders of sexual development

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Authors' contributions
AA collected, analysed, and interpreted the patient data and was a contributor in writing the manuscript. A.F, S.H, S.K, and K.S.A wrote and revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Approval was obtained from the research ethics committee of the Faculty of Medicine, Cairo University. Written informed consent was obtained from the parents.

Consent for publication
Written consent to publish had been obtained from the parents.

Competing interests
The authors declare that they have no competing interests.

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