



One –Stage Feminizing Genitoplasty in Patients with Congenital Adrenal Hyperplasia

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Background/ Purpose: A growing interest has been noted recently in one -stage Feminizing genitoplasty for patients with congenital adrenal hyperplasia (CAH). The timing of surgery is currently controversial. This study was carried out to investigate the feasibility and outcome of one –stage feminizing genitoplasty at various ages.

Materials & Methods: Eighteen female patients with CAH were treated during a six year-period. All patients undergone one- stage clitoroplasty, vaginoplasty, and labioplasty. Fifteen with high or intermediate confluence of vagina and urethra underwent total urogenital mobilization (TUM). A perineal posterior flap vaginoplasty and minimal mobilization of the urogenital sinus (UGS) was adequate in 3 cases with short UGS. Each patient was evaluated as regard to age at surgery, degree of virilization, preoperative diagnostic studies, operative technique, and outcome. Follow up ranged from 2 to 72 months.

Results: Patients aged 5 weeks to 6 years. Mean operative time was 180 minutes (range: 120 to 230 minutes). The dissection was technically easier, and the mean operative time was shorter in patients younger than 6 months at time of surgery compared to older children (140 versus 200 minutes). Postoperative complications included: atrophy of the clitoris (n= 2), absent labia minora (n=2), and vaginal stenosis (n=4). Fecal and urinary continence were documented in 9 of 10 children who are older than 3 years. The cosmetic and anatomic outcomes were considered good or satisfactory in 16 of the 18 patients (88.9%).

Conclusion: One-stage feminizing genitoplasty is both feasible and safe in patients with CAH. Total urogenital mobilization technique has tremendously simplified the feminizing genitoplasty even in patients with high confluence of vagina and urethra. The repair is technically much easier in young infants.

Index Word: Intersex, congenital adrenal hyperplasia, genitoplasty

INTRODUCTION

Congenital adrenal hyperplasia (CAH) is the most common cause of ambiguous genitalia in the newborn with an estimated incidence of 1 in 14000 live birth.¹ Female patients with CAH have one of several enzymatic defects which results in a significant increase of androgens and variable degrees of virilization. Salt-losing metabolic disturbance occurs in three quarter of these cases.² Elongation of

the clitoris and fusion of labio-scrotal folds results in a clinical picture of postnatal ambiguous genitalia. The urogenital sinus (UGS) may be elongated and often in an abnormal location on the perineum or phallus.³ The vagina and urethra open into urogenital sinus rather than separately on the perineum. The level of the vaginal entry into the urogenital sinus may be determined by the level of exposure to adrenal

androgens in utero. Higher exposure was proposed to lead to a more proximal entry of vagina into the urogenital sinus.⁴

The objective of surgical reconstruction is the separation of the urinary and genital tracts allowing for normal voiding, creation of an adequate vaginal introitus and achievement of a near normal appearance of the external genitalia.⁵ these objectives can be achieved by removing the corpora and preserving the glans with its innervation to create a clitoris with normal sensation; creating a normal-appearing introitus by fashioning labia minora from phallic skin and foreskin; and vaginoplasty to provide an adequate opening for the vagina onto the perineum.⁶

In the past, genitoplasty and vaginoplasty, were commonly performed as separate, staged procedures. A growing interest in one -stage feminizing genitoplasty that includes clitroplasty, labioplasty and vaginoplasty was noted recently.⁵⁻⁹ The timing of surgery in those patients is one of the many factors that influence outcome and is currently controversial.¹⁰ Many surgeons prefer to do corrective genital surgery early.^{9,10} On the other hand others prefer to defer surgery until patients are old enough to give informed consent.¹¹

The purpose of this study was to evaluate the feasibility and outcome of one -stage feminizing genitoplasty at various ages.

MATERIALS AND METHODS

Eighteen female patients with CAH were treated at the division of Pediatric Surgery, Tanta University Hospitals and affiliated Hospitals during the period from 2000 – 2006. The degree of virilization was assessed in all patients by meticulous examination of the external genitalia. Mild virilization was defined as incomplete labial fusion, urogenital sinus opening between the labia majora and mild clitoral hypertrophy. Moderate virilization was characterized by complete labial fusion, urogenital sinus opening near the base of phallus and moderate clitoral hypertrophy. Severe virilization was classified as complete labial fusion; urogenital sinus opens near the tip of the phallus with gross clitoral hypertrophy.

Diagnostic workup included blood electrolyte and steroid measurement. Radioimmunoassay of plasma 17-hydroxyprogesterone was used for the diagnosis of 21-hydroxylase deficiency; while

increased plasma levels of 11-deoxycortisol was used as a marker for 11 β -hydroxylase deficiency. High levels of potassium and low level of serum sodium indicated salt loosing type.

All patients undergone abdominal and pelvic ultrasound. Retrograde flush genitogram was performed by insertion of a Foley catheter into the distal opening followed by low pressure injection of a water soluble contrast agent under fluoroscopy. The site of confluence of the urethra and vaginal was determined. The length of the proximal urethra and urogenital sinus, and the size of vagina were noted (Fig.1).

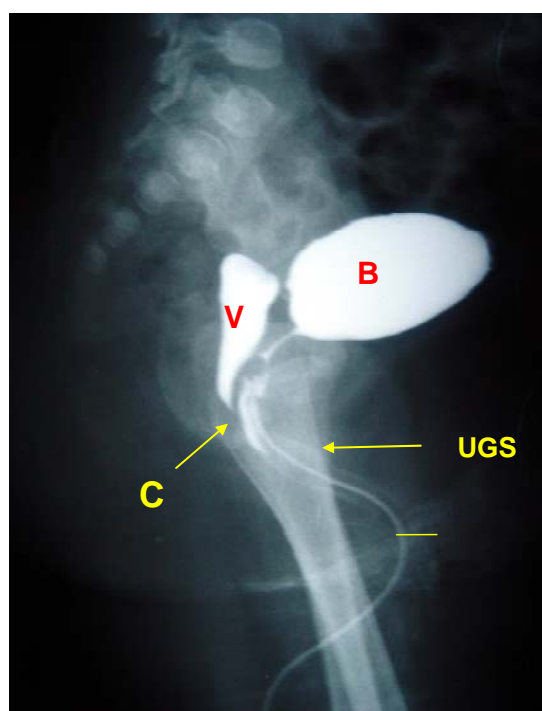


Fig 1. Retrograde flush genitogram showed the site of confluence (c) of the urethra and vagina, long urogenital sinus.

Chromosomal analysis was done for confirmation of the genotypic sex. Laparoscopy was done in 6 patients. Seven patients underwent pandendoscopic examination of the genitourinary tract to identify the vaginal opening and its relationship to the external urinary sphincter.

An informed consent for feminizing genitoplasty was taken in each case after detailed discussion with parents. Preoperative preparation was made and included doubling of the corticosteroid dose.

Surgical technique:

The child was placed in a supine position with both legs attached to an inverted U shape bar fixed at the end of the operating table. Pandendoscopic examination was done at this stage.

Clitroplasty

The clitoral reduction was performed in 15 patients. Clitoral recession was done in the remaining 3 patients with relatively mild enlarged clitoris. A 4/0 traction suture was placed into the glans of the clitoris. A circular incision was made just proximal to the glans. The dorsal skin was completely degloved to the base of the clitoris, and was incised at middle to create two flaps which were used to construct the labia minora or lateral wall of the vagina (Fig 2). Two methods were used for clitoral reduction. The first one was used in 3 patients where neurovascular bundle was dissected free to the glans followed by excision of the 2 corpora and leaving the glans with its intact blood supply through the neurovascular bundle. In the subsequent 12 patients, Kogan technique was used to protect all neurovascular elements to the glans.¹² Two incisions were made at lateral side of both corpora. Only the erectile tissues were excised. The glans of the clitoris was reduced if needed and then fixed to the lower border of symphysis pubis. (Fig 2 C)

Vaginoplasty

A posterior inverted U- shape skin flap was prepared keeping the flap base narrow. The apex of the flap touched the posterior rim of the UGS opening. An incision was made circumscribing the sinus, which mobilized circumferentially. The dissection extended anteriorly to the upper border of the symphysis pubis, posteriorly to the peritoneal reflection and laterally to above the levator ani muscles. The UGS was then incised posteriorly and the incision was extended into the posterior vaginal wall. The apex of the posterior skin flap was sutured to the corner of the vaginal incision. The distal free end of the open UGS was sutured to the posterior aspect of the clitoris. (Fig 2)

In cases with very high confluence of the vagina and urethra, the vagina did not reach the perineum despite TUM. In these cases, the posterior wall of the

vagina was opened, the anterior wall of vagina was very carefully separated from the urethra for a 0.5 to 1 cm, and the vaginal opening into UGS is closed using 6/0 Vicryl sutures. The distal part of a long UGS is incised at 12 O'clock and reflected ventrally to reconstruct the anterior wall of the vagina. The proximal part of UGS was used as urethra. The 2 dorsal skin flaps of the clitoris were used to construct part of the anterior and lateral walls of the vagina. The posterior wall was constructed using the inverted U shape posterior perineal skin flap. Vaseline gauze was used as a vaginal pack, and removed after 48 hours (Fig 3).

Labioplasty

After suturing the flaps to the vagina, the skin of the labia majora was advanced inferiorly until it reached the base of the inverted u-flap (Fig 3F& 4B). A bladder catheter was kept in place for 2-3 days in the post operative period. A vaginal stent was used in only 3 cases.

All patients received a third generation cephalosporine for 5 days after surgery. Analgesics were given during the first postoperative 24 hours. Oral feeding was permitted within 24 hours after surgery. Vaginal calibration was done during each postoperative visit to ensure adequacy of the size of the vagina. Regular vaginal dilation was done only if stenosis developed.

The postoperative cosmetic and anatomic results were evaluated according to Creighton et al,¹¹ and Lean et al¹⁰ scores for genital proportions and symmetry, clitoral size and position, vaginal introitus, and labial appearance and proportions (from normal, scrotalized, partial fusion to total fusion), pubic hair distribution, and genital skin quality. Overall cosmetic outcomes were then assigned to categories of good (genital appearance normal, unlikely to be judged abnormal by a non-medically trained person), satisfactory (up to 2 minor abnormalities, unlikely to be judged abnormal by a nonmedically trained person) or poor outcome (genitalia appear abnormal; 3 or more abnormal features).¹⁰

The functional results were evaluated according to the degree of bowel control, urinary voiding pattern, and size of the vagina. Follow up ranged from 2 to 72 months



Fig 2A. Preoperative photograph of a two-month old patient with salt losing CAH



Fig 2B. Degloving of dorsal skin of the enlarged clitoris. The clitoral skin flaps are used to construct labia minora

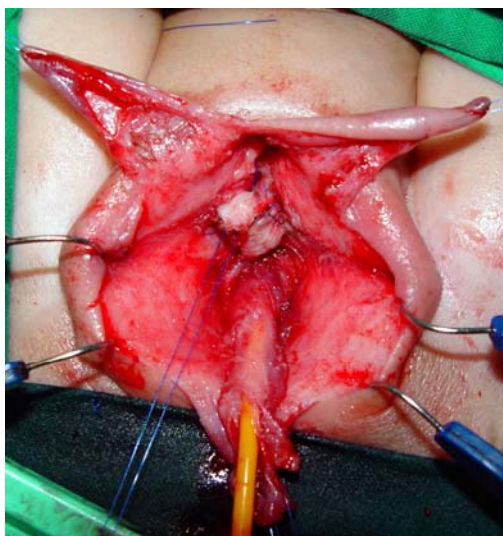


Fig 2C. Clitoral reduction, and UGS mobilization

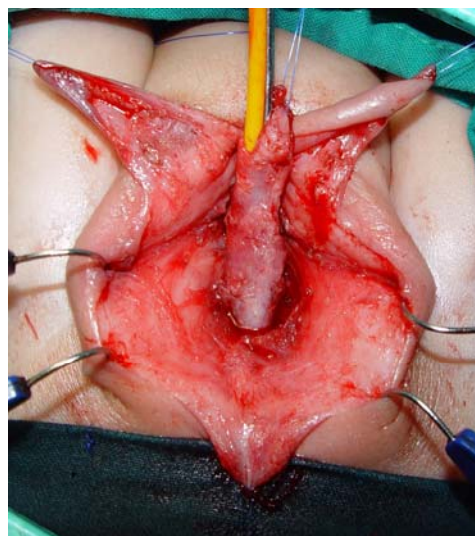


Fig 2D. UGS mobilization.

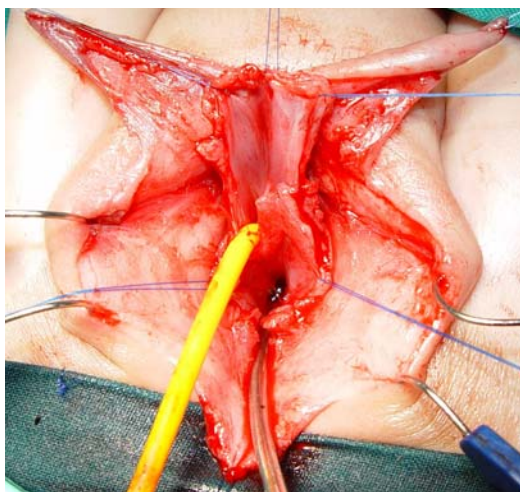


Fig 2 E. The UGS is incised posteriorly and incision is extended into posterior vaginal wall. The sinus is sutured to posterior aspect of clitoris.



Fig 2F. Clitoroplasty, vaginoplasty, and labioplasty are completed. The urethral opening is accessible (catheter is inserted)



Fig 3A. An 11- month old female infant with non salt losing CAH (11 β -hydroxylase deficiency). Complete fusion of labia and extension of the UGS to the tip of a completely virilized clitoris is noted. The patient has been raised as a boy and presented for bilateral impalpable testes.



Fig 3B. Skin incision is made for degloving of clitoral skin and for preparation of a posterior inverted U shaped perineal skin flap.

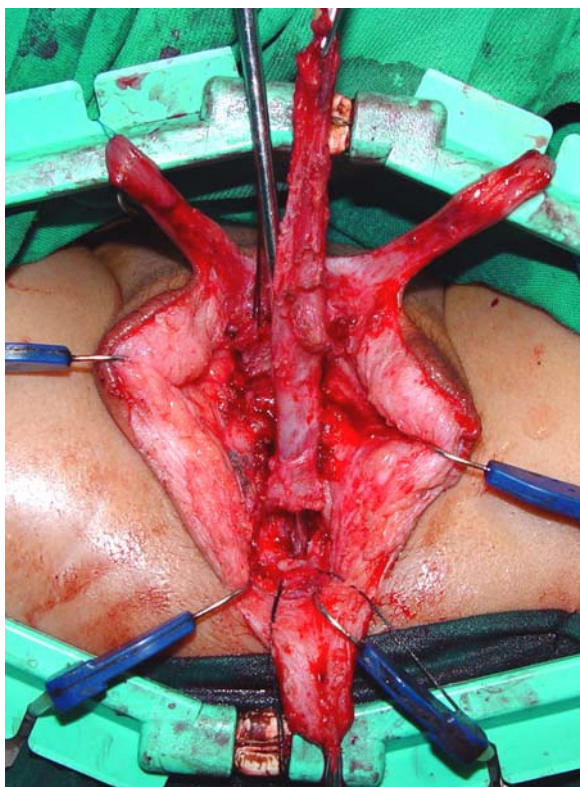


Fig 3C. Kogan's reduction clitoroplasty and total urogenital mobilization is completed. A very long UGS is shown. The posterior wall of the high vagina is opened just proximal to its junction with urethra. A catheter is shown in vagina

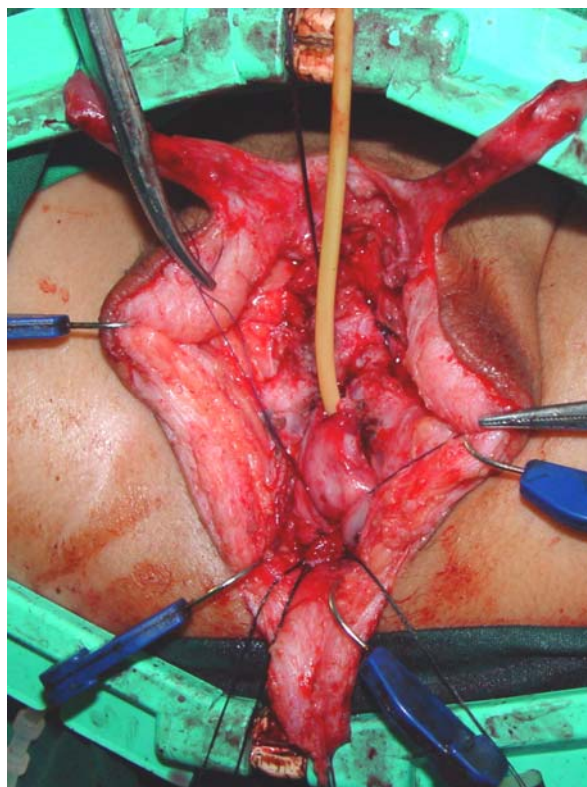


Fig 3D. The distal part of the UGS is spilted leaving its proximal part to increase urethral length. The spilted part of UGS is inverted and sutured to the short anterior and lateral vaginal walls.

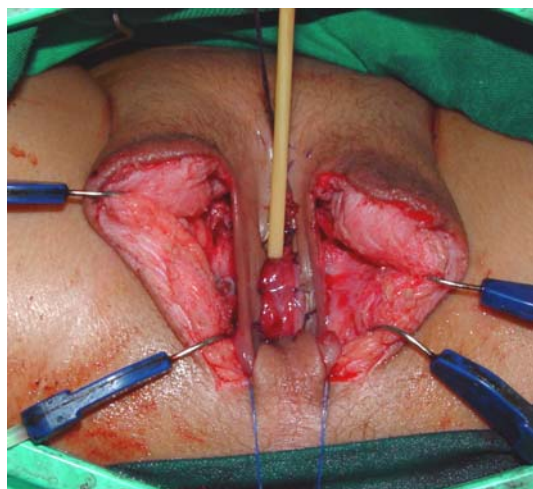


Fig 3E. The inverted U shaped perineal skin flap is used to construct posterior vaginal wall. The long clitoral skin flaps are used to construct the labia minora



Fig 3F. The labial scrotal folds are transposed to create labia majora. A vaginal vaseline pack is left for 48 hours.



Fig 3G. The same patient 2 years after feminizing genitoplasty with good cosmetic and anatomic outcome

RESULTS

The Age of patients ranged from 5 weeks to 6 years (Table 1). Eight patients were less than one year of age at time surgery, while 6 were older than 3 years. Two patients had mild virilization, 7 showed moderate virilization, while 9 presented with severe virilization.

Table 1. Age of patients at surgery

Age	No (%)
< 3 months	3 (16.7%)
3-6 Months	3 (16.7%)
6-12 months	2 (11.1%)
1-3 years	4 (22.2%)
> 3 years	6 (33.3%)

Preoperative diagnostic workup:

Blood chemistry and hormonal assay revealed that 21-hydroxylase deficiency with an elevated plasma levels of progesterone and 17-hydroxyprogesterone in 15 patients, while 3 had 11 β -hydroxylase deficiency with marked increased plasma levels of 11-deoxycortisol. Twelve patients proved to be of salt loosing type as noted from the high serum levels of potassium and low sodium levels.

Karyotyping confirmed female genotype (46 XX) in all patients. A pelvic ultrasound study showed the presence of müllerian structures in only 14 of the 18 patients (77.8%). Ultrasound failed to show uterus in 4 patients. Laparoscopy confirmed the presence of normal internal female structures in these later 4 patients. Retrograde flush genitogram successfully showed the site of confluence of the urethra and vagina in 5 of 9 studies. Pandendoscopic examination of the genitourinary tract identified the vaginal opening and its relationship to the external urinary sphincter in all these 7 patients.

Three patients had low insertion of the vagina into a short UGS. They required minimal mobilization of the UGS, and were treated with clitoroplasty and simple posterior flap vaginoplasty. The remaining 15 patients with either high or intermediate confluence required TUM. Mean operative time was 180 minutes (range: 120-230 minutes). The mean operative time was shorter in patients < 6 months of age compared to older children (140 versus 200 minutes). Likewise, the dissection was much easier, and blood loss was



Fig 4 A . Preoperative appearance of the external genitalia of a 16- month old female patient with CAH



Fig 4B. One-stage feminizing genitoplasty: A urinary catheter is inserted. Another catheter and vasline gauze pack are inserted in the reconstructed vagina



Fig 5 A . Preoperative appearance of the external genitalia of 6 year old female patient with CAH. Severe virilization and pigmentation is shown



Fig 5 B . Two weeks after one-stage feminizing genitoplasty: The labia minora was constructed from the skin of the clitoris



Fig 6 A. Preoperative appearance of the external genitalia of 12 month old female patient with CAH.



Fig 6 B. Six months after one-stage feminizing genitoplasty: The skin of labia majora is still scotalized, but the clitoris and vagina are satisfactory.

minimal in younger children. No blood transfusion was required. All patients were discharged home within 3-4 days after surgery.

There were no changes in voiding pattern postoperatively in those patients who were toilet trained before surgery. Fecal and urinary continence were documented in 9 of 10 children older than 3 years at recent follow up. A five - year old girl continued to have incontinence of urine especially during crying or straining.

The anatomic and cosmetic results are shown in Table 2&3. The overall cosmetic appearance of the introitus was good or satisfactory in all except 2 patients who had small labia majora with posteriorly located narrow vaginal orifice (Fig.5- 6). The urethral meatus was situated in the vestibule and easily accessible in all except one patient.

Postoperative complications included: complete atrophy of the clitoris in 2 patients, absent labia minora in 2 patients, and vaginal stenosis in 4 patients who respond to repeated dilatation.

Table 2. Anatomic and cosmetic outcomes of 1-stage feminizing genitoplasty

	Normal	Abnormal
Clitoris size	13	5 (1 large, 2 small, 2 absent)
Clitoral position	15	3(1 low, 2 absent)
Vaginal introitus	15	3 (small)
Introital position	16	2 (not surrounded by labia majora)
Labia majora	14	4 (1 small, 3 scrotalized)
Labia minora	14	4 (1 small, 1 poor, 2 absent)

Table 3. Overall Anatomic and cosmetic outcomes after planned 1-stage reconstruction

Overall cosmetic and anatomic result	No (%)
Good	12 (66.7%)
Satisfactory	4 (22.2%)
Poor	2 (11.1%)

DISCUSSION

The adrenogenital syndrome caused by CAH is a classic example of an inborn error of metabolism in

this case, an error involving cortisol synthesis. The most commonly deficient enzymes are 21-hydroxylase or 11-hydroxylase. A deficiency of steroid 21-hydroxylase is responsible for 95% of cases of CAH.¹ Although most of our patients were due to 21-hydroxylase deficiency (n=15, 83%), a significant percentage (17%) were due to 11 β -hydroxylase deficiency. This difference may be attributed to the relative small number of patients in our series or may reflect a real higher percentage of 11 β -hydroxylase deficiency in our geographic area. More number of patients will be needed to finally declare the types of enzymatic deficiency in our local population.

Abdominal ultrasonography was reported to have a 100% sensitivity and specificity in the identification of internal female genitalia.¹³ Ultrasonography can also provide adequate information about the anatomy of the vagina and UGS in more than 90%.¹³ In our study, the accuracy of Ultrasonography in detection of internal mullerian structures were only 77.8%. The sensitivity was low in neonates and young infants. The experience of the radiologist and/ or the quality of ultrasographic machine may explain this low sensitivity.

In contrast to ultrasonography, retrograde genitography has been constantly reported to be less accurate in identifying the site of communication between the vagina and urogenital sinus. Chertin et al¹³ reported that retrograde genitography was accurate in only 60% patients. A similar low accuracy rate (5 of 9, 55.6%) was noted in our study. Laparoscopy proved to be very sensitive and specific tool in visualizing internal female structures. Genitourinary panendoscopy was the most accurate method to locate the entry of vagina into UGS in this study. This step is recommended whenever feasible before starting genitoplasty.

Several techniques have been described for vaginal reconstruction during the last few years.¹⁴⁻²⁰ A cut back of the urogenital sinus combined with Fortanoff inverted U-shape perineal flap is used in cases with low confluence of the vagina and urethra.²¹ However, use of this technique is inappropriate when the confluence is higher because it leaves the urethral meatus on the anterior vaginal wall, resulting in accumulation of urine in the vagina.

When the vagina enters the urogenital sinus proximal to the external urethral sphincter, cut back of the urogenital sinus should be avoided to prevent division of the sphincter; instead, the vagina is

dissected free from the urethra and brought down posteriorly. Separation of the vagina from the urethra and bringing it out onto the perineum is technically demanding. Total urogenital mobilization technique for repair of intermediate length cloaca as described by Pena has the advantage of avoiding the dissection required for separation of the vagina from the urethra.²² Both the vagina and urethra are mobilized together and brought to the perineum. In 1999, Ludwikowski et al demonstrated the feasibility of performing this technique in children without anorectal malformation through a perineal approach, but they discarded the mobilized UGS and created a separate urethral meatus and vaginal introitus.¹⁸

In this study TUM has tremendously facilitated the genitoplasty. Contrary to Ludwikowski et al we did not discard the mobilized UGS, but we use it in all cases. The UGS was split at 6 O'clock orientation and reflected upwards to enlarge the introitus in patients with low confluence, this allows the best mucosal lining and reconstruction of the valvular region. This approach was supported by other investigators in recent literature.⁵⁻¹⁹

The length of the urethra proximal to the confluence of the vagina and UGS is important.⁹ It is generally believed that there is correlation between the severity of virilization and the proximal migration of the junction of the vagina and UGS.⁴ Jenak et al⁵ applied TUM technique only when the urethra appears normal. They reported that, when the urethra is too short the risk of incontinence is high and therefore, they use a technique that preserve the urogenital sinus as a urethra and the vagina is then reconstructed using a skin flaps.⁵ However, other investigator showed that the location of the vaginal entry into the urethra remains at a constant distance from the bladder neck at various degrees of virilization.²³ In this study, we found that TUM technique is very beneficial in severely virilized patients with expected short urethral length proximal to the confluence. After completing TUM, the distal part of the UGS was incised and reflected posteriorly to repair the anterior wall of the vagina, while its proximal part was used as a urethra.

Several techniques were described for clitoroplasty.¹²⁻²⁴ The clitoral recession which was common in the past has been replaced by clitoral reduction in order to avoid the complication of potential re-growth of the clitoris and also to avoid painful erection. We noted that Kogan technique of clitoral reduction is a safe technique because it

assures the preservation of blood supply to the glans. The 2 cases of complete clitoral atrophy in our series occurred after free isolation of the neurovascular bundle to the glans.¹²

Having a planned single stage procedure seems to give a better outcome than multistage genital surgery; with an expected 88% incidence of good cosmetic results.¹⁰ Repeated surgery may cause more scarring and fibrosis. In our community this sort of surgery is very embarrassing to the patients and their parents. We noted that accomplishing genitoplasty as one stage operation at early infancy was very much appreciated from the parents.

A great deal of controversy remains surrounding the proper time of surgery. Most investigators suggest that intervention should take place early from the newborn to 3-year-old period.²⁵ Reasons for this early intervention include better compliance with dilatation, lessening of parents concerns regarding their child and the assumption that the child later in life does not remember early intervention.²⁶ Many additional arguments have been proposed for early surgery, including avoidance of genitourinary tract infection⁴ and relative ease of surgery in childhood compared with adolescence.²⁷ Lobe et al reported better results in patients diagnosed and operated during infancy.²⁸ Passerini-Galzel reported that surgery can be performed easily in the first 1 to 2 months of life but some revision at puberty should be anticipated in some cases.²⁵ In the current series, the technique was much easier in two patients < 6 months of age compared to older children as evident by shorter operative time. The psychological benefit of early vaginoplasty versus the possible need of some revision after puberty should be considered. In patients with CAH and other conditions that involves abnormal-appearing genitalia, the benefits of early intervention outweighs the risks of repeated dilatation at a younger age.²⁶ Deferring definitive vaginoplasty until puberty, especially when virilization is associated with a high or intermediate vagina, is still supported by other investigators,^{29,30} who claim the availability of supple, more robust genital skin in adolescent and adult than in infants. Also vaginal dilatation if needed is more likely to be successful when undertaken regularly by motivated young women than when imposed on an incomprehensible child. In our study, we noted that the vagina was easy to handle and not thin and fragile in the young infants. Likewise, postoperative regular vaginal dilation is not mandatory in every patient.

The late results of feminizing genitoplasty have been systematically documented in the literature.³¹⁻³⁵ Vaginal stenosis is the most commonly reported complication occurring in up to 78% of cases.³¹ Vaginal stenosis can be either extrinsic or intrinsic. Extrinsic stenosis is mainly a consequence of poor anatomical preparation of the perineal structures, while intrinsic stenosis is due to primarily to inadequate opening or excision of the distal part of a high vagina which is fibrotic and dysplastic.²⁵ In our series, vaginal stenosis was noted in 4 out of 18 patients who responded to repeated dilatation. In order to minimize the frequency of postoperative vaginal stenosis, Passirini-glazel²⁵, and Rink et al³² advocated deeply incision of the distal part of the vagina until a wide vaginal lumen is entered. A perineal inverted U-shape Fortunoff flap is used to connect the wide vaginal lumen with the perineal surface.³⁶ According to some investigators, if stenosis occurs vaginal periodic dilatation or reoperation can be postponed until puberty to take the advantage of the hormonal stimulus that occurs during this phase and also to minimize the psychological effects of multiple procedures.^{25, 32}

The main goal of performing feminizing genitoplasty at an early age is to create normal looking external genitalia that will allow the child to grow up normally. For this reason assessment of the cosmetic result is very important for both the patients and the family. The cosmetic and anatomic outcomes were considered good or satisfactory in 88.9% of our patients. Similar to our results, in a series of 27 females underwent an one-stage feminizing genitoplasty, Miranda et al³⁶ reported an excellent or good in 63% of the cases, satisfactory in 18.5% and unsatisfactory or bad in 18.5%. However, the results from Creighton et al¹¹ are in marked contrast to our results. Using objective measures, they judged that 41% had poor cosmetic results, with 89% of the women who had had planned 1-stage procedures requiring further major surgery. In a series of 16 patients treated with 1-stage procedure, Lean et al¹⁰ found that only one patient required further major surgery. Apart from dilatation, none of our patients required further surgical treatment. It is not certain that any of them will need a revision surgery such as labial refashioning or introital enlarging procedures when they reach puberty.

CONCLUSION

Early one -stage genitoplasty can be used safely and effectively to provide adequate introitus with excellent cosmetic appearance. The procedure is much easier in young infants with less blood loss, shorter operative time and less psychological trauma. The proper technique should be tailored to the severity of the anomaly. Adopting TUM approach has tremendously simplified the feminizing genitoplasty even in cases of high confluence of the vagina and urethra.

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