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Anatomical and cosmetic outcomes following feminizing genitoplasty in patients with disorders of sex development

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Abstract: Background: Objectives: Ambiguous genitalia in the newborn is the commonest presentation of disorders of sexual development (DSD), most commonly secondary to congenital adrenal hyperplasia (CAH), Those patients require feminizing genital reconstruction aiming at 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. The aim of this work was to evaluate the anatomical and cosmetic outcome of feminizing genitoplasty in Patients with disorders of sex development. **Methods:** Twenty patients presented with disorders of sex development admitted to the Pediatric Surgery Unit in Tanta University Hospital, over a period of two years, from June 2016 to June 2018. Genital examination was performed for all patients and the degree of virilization in cases of CAH was assessed according to the Prader scoring system. All patients undergone one- stage feminizing genitoplasty and the Postoperative cosmetic and anatomical outcome was evaluated according to the criteria described by Creighton and colleagues. Follow-up period ranged from 6 to 24months. **Results:** Out of the twenty cases in this study, 18 cases had congenital adrenal hyperplasia, two cases had complete androgen insensitivity syndrome (CAIS). All cases of CAH had a 21-hydroxylase deficiency. The Age of patients ranged between 6 months and 16 years. Seven patients were less than one year of age at time of surgery (7/20[35%]). While6 patients were older than 3 years (6/20 [30%]). The urogenital sinus mobilization which was used in 17 cases (17/18 [94.5%]), The partial urogenital mobilization (PUM) was used in 3 cases (3/18 [16.7%]) and the total urogenital mobilization (TUM) was used in 14 cases (14/18 [77.7%]) while colon vaginoplasty was used in the two cases of CAIS and one case of CAH. Our anatomic and cosmetic outcomes were good in 17(85%) for those patients initially treated at our institute by our specialized team, satisfactory in 2(10%) and poor in1(5%). **Conclusions:** Feminizing genitoplasty can be used safely and effectively with good anatomical and cosmetic outcome provided that the pediatric surgeon is familiar with the procedure. The feminizing genitoplasty is technically much easier in young infants. Sigmoid vaginoplasty is a good choice in cases of CAIS and CAH where the vaginal confluence was high close to the bladder neck and the vagina was very short.

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Key words: Feminizing genitoplasty, congenital adrenal hyperplasia, complete androgen insensitivity syndrome.

1. Introduction

Disorders of sex development (DSD) refer to a spectrum of congenital conditions in which there is biological discrepancy between chromosomal, gonadal, and phenotypical sex and they are among the most challenging conditions confronting the paediatric surgeon and endocrinologist. [(1)]

Ambiguous genitalia in the newborn being the commonest presentation of disorders of sexual development (DSD), demands urgent and exact diagnosis, most commonly secondary to congenital adrenal hyperplasia (CAH). [(2)]In these patients there is a persistent communication between the urethra and vagina, which results in a common urogenital perineal channel, the Urogenital (UG) sinus with longation of the clitoris and fusion of labio-scrotal folds results in a clinical picture of postnatal ambiguous genitalia. [(3)]

The objective of feminizing 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. 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. [4]

The timing of surgery in patients with genital anomaly is one of the many factors that influence outcomes and is currently controversial. Current practice in many institutions, including our own, is to do corrective genital surgery when the child is young. However, poor outcomes reported in some centres have led to questioning of the appropriateness of early surgical intervention and suggestions that it would be better to defer surgery until patients are old enough to give informed consent. [5]

The purpose of this study is to evaluate the anatomical and cosmetic outcomes of feminizing genitoplasty in patients who have been treated through one institution in Tanta university, Egypt, using the criteria described by Creighton et al. [5]

2. Patient and methods

This study included twenty patients presented with disorders of sex development admitted to the Pediatric Surgery Unit in Tanta University Hospital, over a period of two years, from June 2016 to June 2018, were managed by feminizing genitoplasty.

Out of the twenty cases in this study, 18 cases had congenital adrenal hyperplasia, two cases had complete androgen insensitivity syndrome (CAIS). All cases of congenital adrenal hyperplasia had a 21-hydroxylase deficiency. Genital examination was performed for all patients and the degree of virilization in cases of CAH was assessed according to the Prader scoring system. [6]Diagnostic workup included estimating the level of blood electrolytes to detect cases of the salt-losing type and steroid measurement, High plasma levels of 17- hydroxyprogestrone were indicative of 21-hydroxylase deficiency, Chromosomal analysis was done for confirmation of the genotypic sex. An abdominopelvic ultrasound was performed to evaluate internal sex organs. All patients had undergone a retrograde flush genitogram for delineation of the anatomy of the urogenital sinus, vagina and level of confluence. **(Fig.1)** Laparoscopy was done in cases of CAIS patients. Panendoscopic examination of the genitourinary tract was performed immediately prior to surgery to introduce balloon catheters in both the urethra and vagina. Also to confirm the anatomy of the urogenital sinus and level of vaginal confluence especially in patients in whom evaluation of anatomy by imaging was difficult. An informed consent for feminizing genitoplasty was taken in each case after detailed discussion with parents. Preoperative preparation was made with doubling of the corticosteroid dose on the morning of the operation.

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

Surgical Technique:

Surgical correction aimed at full correction using the most suitable tailored technique for each case. Clitoral reduction, labioscrotal reduction, and exteriorization of the vagina were done together. 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. Clitoral reduction was performed in 16 cases (16/18 [88.8%]). Using the Kogan technique. [7] of subtunical excision of the two corpora leaving the glans with the intact neurovascular bundle. In two cases (2/18 [11.2%]) this was not used due to previous surgical excision during circumcision in one case and previous surgical reduction in the other case. The dorsal skin of the clitoris after degloving was incised at middle to create two flaps which were used to construct the labia minora or lateral wall of the vagina **(Fig.2) As regard to vaginoplasty** An inverted U-shaped flap was marked and incised reaching anteriorly to the edge of the sinus and posteriorly to the posterior margin of the new labia. An incision was made around the sinus, which mobilized circumferentially. The dissection extended anteriorly to the upper border of the symphysis pubis, posteriorly to the peritoneal reflection by dividing the attachments between the urogenital sinus and the rectum. **(Fig.2)** The urogenital sinus (UGS) mobilization was used in 17 cases (17/18 [94.5%]), The partial urogenital mobilization (PUM) was used in 3 cases (3/18 [16.7%]) in which 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 to create a mucosa lined vestibule.

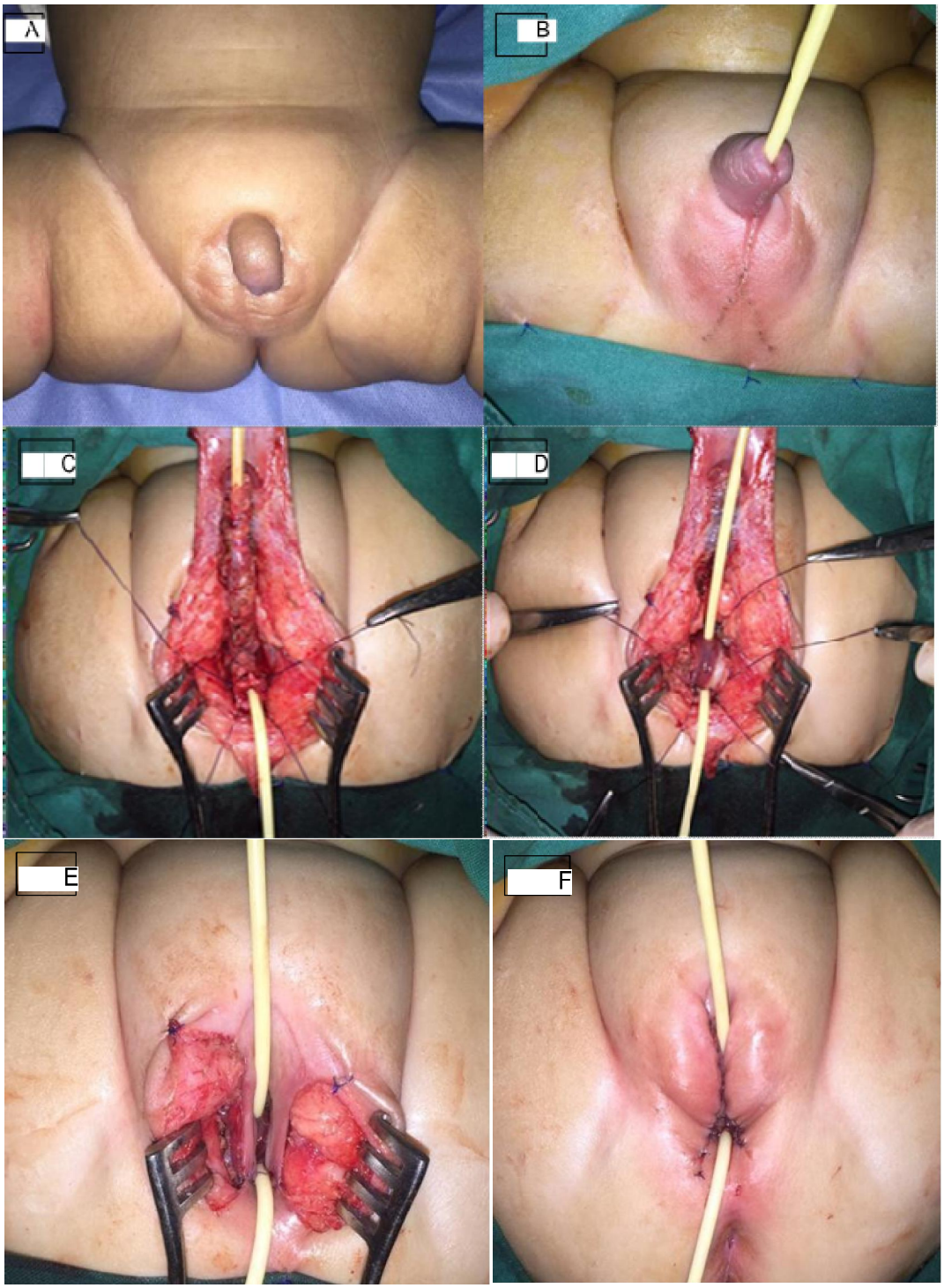

Fig. (2): A: Preoperative photograph of a 7 month old patient with CAH. **B:** marking incision by fine needle diathermy with posterior perineal flap. **C:** total urogenital mobilization is completed. A very long UGS is shown. The posterior wall of the high vagina is opened just proximal to its junction with urethra. A catheter is shown in vagina. **D:** The distal part of the UGS is spilited leaving its proximal part to increase urethral length. The spilited part of UGS is inverted and sutured to the short anterior and lateral vaginal walls. **E:** 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. **F:** Clitoroplasty, vaginoplasty, and labioplasty are completed. The uretheral opening is accessible (catheter is inserted).

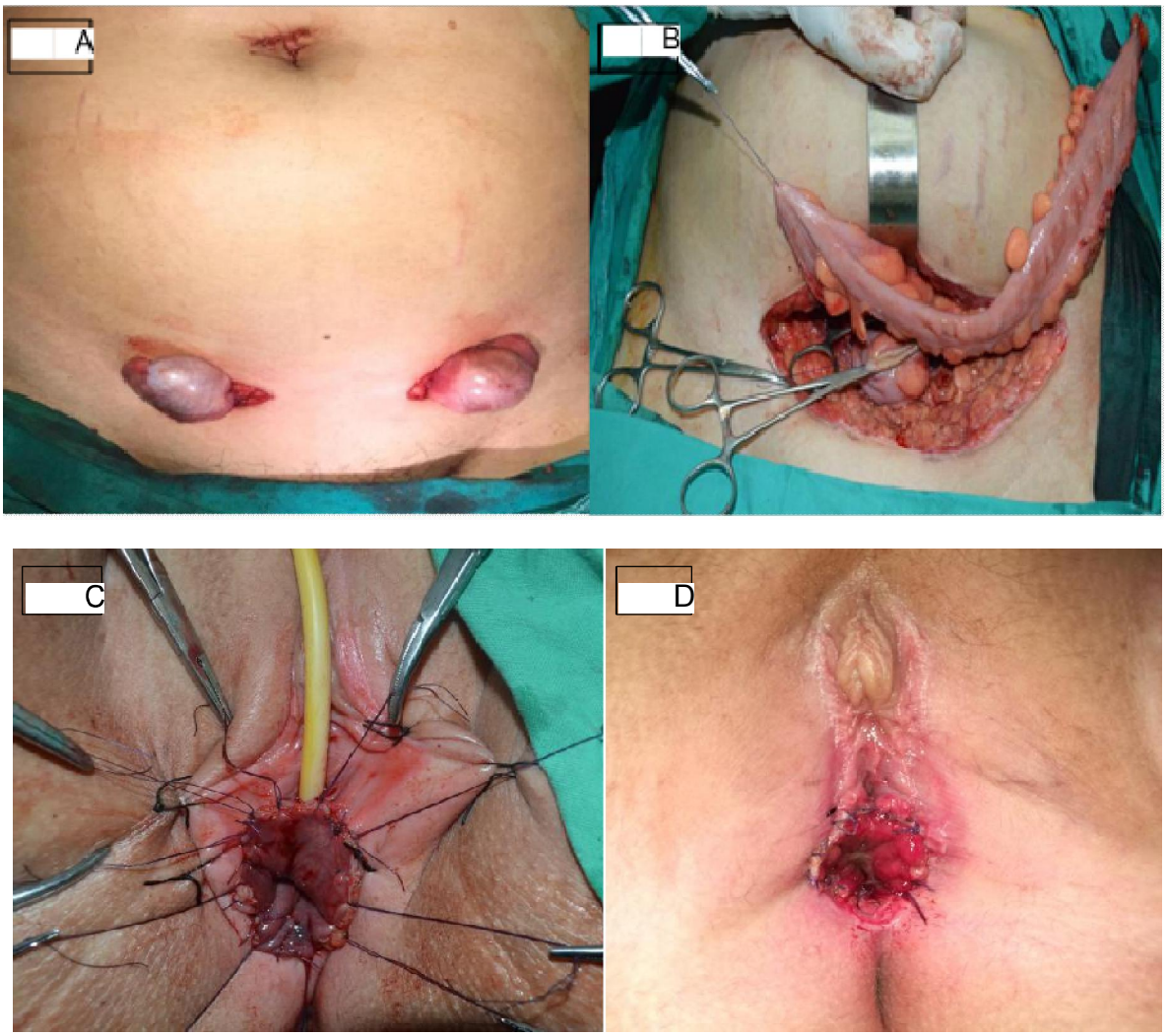

Fig. (3): A: A case of complete androgen insensitivity aged 18 year with bilateral inguinal testes. **B:** Colon vaginoplasty of the same case using 15cm loop of sigmoid with preserved blood supply. **C:** A single layer colovestibular anastomosis behind the urethral opening. **D:** One month postoperatively showing good introitus.

While the total urogenital mobilization (TUM) was used in 14 cases (14/18 [77.7%]) with very high confluence of the vagina and urethra, the vagina did not reach the perineum despite TUM. In these cases, a pull-through type procedure was performed. the anterior wall of vagina was very carefully separated from the urethra 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 dorsally 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. (Fig.2) In cases of testicular feminizing syndrome and one case of congenital adrenal hyperplasia where the vaginal confluence was high close to the bladder neck and the vagina was very short we did colon vaginoplasty using a segment of the sigmoid colon. The technique involved laparotomy through a Pfannenstiel incision. A 10 to 15cm segment of the sigmoid colon was isolated preserving the blood supply. In cases of testicular feminizing syndrome one end was closed in two layers to form the vertex of the neovagina, and the other end was left open to act as the neovaginal orifice. The continuity of the colon was re- established. The vaginal tract was bluntly dissected between the bladder and rectum to the level of the peritoneal reflection. The open sigmoid loop was pulled down into position. A single-layer anastomosis was performed in the hymnal region. In the case of

congenital adrenal hyperplasia the same technique was used but the segment of colon was used as an interposition flap. The upper end was anastomosed to the remnant of the vagina and the lower end was anastomosed to the perineum behind urogenital sinus, which was left as the urethra. (Fig.3) AS Regard to the Labioplasty, The labioscrotal tissue was widely mobilized, trimmed, and moved posteriorly as a Y-V plasty to create labia majora lateral to the vaginal orifice. This V-Y reconstruction of the labioscrotal folds into a labia majora was achieved effectively in 16 cases (16/18 [88.8%]). It was needed minimally in 2 cases (2/18 [11.2%]), where the labioscrotal folds were minimally hypertrophied A Foley's catheter was left in the urethra and removed after 5 -7 days. Vaseline gauze was used as a vaginal pack, and removed after 48hours. Oral feeding was initiated within 24 h postoperatively. An appropriate analgesic is administered for pain control in the immediate postoperative period. Broad spectrum antibiotics were administered for the whole period of catheterization. The follow-up period ranged from 6 to 24 months. The postoperative cosmetic and anatomic results were evaluated according to criteria described by Creighton et al (5). Which included the 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 non-medically trained person) or poor outcome (genitalia appear abnormal; 3 or more abnormal features).

3. Results

Out of the twenty cases in this study, 18 cases had congenital adrenal hyperplasia, two cases had complete androgen insensitivity syndrome (CAIS). All cases of congenital adrenal hyperplasia had a 21-hydroxylase deficiency. Of the 18 cases of 21-hydroxylase deficiency, 16 cases were salt wasting (SW) and 2 cases were of the less severe simple virilizing (SV). The Age of patients ranged between 6 months and 16 years. Seven patients were less than one year of age at time of surgery (7/20 [35%]). While 6 patients were older than 3 years (6/20 [30%]). A significant proportion of our CAH cases ranged between Prader's IV and V degrees as shown in **(**Table**1).**

Table (1): Virilization according to prader's score

Virilization (Prader Degree)	Number (18)
II	**1**
III	**3**
IV	**8**
V	**6**

The genitography and cystoscopy findings were matching and provided similar information regarding the site of vaginal entry and hence the operative difficulty in two thirds of the cases (number: 12/18[67%]). However, the cystoscopy excelled the genitography in anticipating the operative difficulty in 6 cases (number: 6/18 [33%]). In all these cases the cystoscopy expected a more proximal vaginal entry and was found to meet the operative findings better than the genitography.

Cosmetic and anatomic outcome of external genitalia after feminizing genitoplasty was evaluated according to criteria described by Creighton et al as shown in **(Table 2)**. The overall cosmetic appearance was good or satisfactory in all except 1 patient who had small labia majora with posteriorly located vaginal orifice **(Table 3).** The urethral meatus was situated in the vestibule and easily accessible in all patients.

There were no changes in voiding pattern postoperatively in those patients who were toilet trained before surgery. A thirteen.

- Year old girl developed stress incontinence of urine during straining. Another patient had dysuria and difficulty of micturition that was only early post-operative findings and did not persist after medical treatment with antibiotics. Wound infection occurred in one patient and was resolved using systemic and topical antibiotics.

Table (2): Cosmetic and anatomic outcome of feminizing genitoplasty.

	Normal	Abnormal
Clitoris size	17(85%)	3(1small(5%), 1absent (5%), 1 large (5%))
Clitoris position	19 (95%)	1absent (5%)
Vaginal introitus	19(95%)	1small (5%)
Introitus position	19(95%)	1(5%) not surrounded by Labia majora
Labia Majora	17(85%)	3(2 redundant (10%), 1scrotalized (5%))
Labia Minora	18(90%)	2(1 poor (5%, 1absent (5%)

Table (3): Overall cosmetic and anatomic outcomes.

	NO (%)
Good	17(85%)
Satisfactory	2(10%)
Poor	1(5%)

4. Discussion

Disorders of sex development (DSD) refer to a spectrum of congenital conditions, in which most patients are identified at birth with genital ambiguity, most commonly secondary to congenital adrenal hyperplasia (CAH). (2) Out of the twenty cases in this study, 18 cases had congenital adrenal hyperplasia, two cases had complete androgen insensitivity syndrome (CAIS). All cases of congenital adrenal hyperplasia had a 21- hydroxylase deficiency. This high incidence of 21-hydroxylase deficiency is similar to the 95% incidence reported in the other studies. [8,9]

In our study, the genitography and cystoscopy findings were matching and provided similar information regarding the site of vaginal entry and hence the operative difficulty in two thirds of the cases (12/18 cases = 67%). However, the cystoscopy excelled the genitography in anticipating the operative difficulty in 6 cases (6/18 cases = 33%). In all these cases the cystoscopy expected a more proximal vaginal entry and was found to meet the operative findings better than the genitography. **Donahoe and Gustafson undermine** the value of genitography as a high confluence may not be identified radiographically and may be noted only on careful endoscopy by a few small punctuate openings at or near an apparently flattened verumontanum. [10] Podesta and Urcullo expressed a similar opinion that combining both investigations gives the best understanding of the confluence depth and proximal urethra. [11]

From our study, we confirm that the key to the different approaches to correct the persistent UGS necessitates extracting as much information about the confluence depth from both investigations to reach the most appropriate surgical decision.

As regards age and timing of surgery in our study, most of our cases were operated before the age of 3 years with 7 cases (35%) before the age of one year, ranging between 6 and 10 months. This study suggested that planned 1-stage surgery gave a better outcome than multistage genital surgery, with 85% of our patients who underwent 1-stage genital surgery having a good cosmetic outcome. In addition, having a single operation also appeared to produce better overall outcomes because repeated surgery may cause more scarring and fibrosis. [12]In our community this type of surgery is very embarrassing to the patients and their parents.

We noted that doing genitoplasty as one stage operation at early infancy was very much appreciated from the parents.

In addition, our results suggested that vaginoplasty can be done before puberty, with minimal intervention required after puberty, and most patients achieved good outcomes with 1-stage feminizing genitoplasty. The best predictors of good outcomes were the institution and well specialized surgeon rather than the age at surgery. Lobe et al reported better results in patients diagnosed and operated during infancy. [13] 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. [14]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. [15]In contrast, Alizai et al. supported postponing vaginoplasty until puberty claiming the availability of supple and genital skin and avoidance of revision after early surgery. [12]

In this study, a significant proportion of our CAH cases ranged between Prader's 4 and 5 degrees of virilization, we had 8 cases (44.5%) of prader 4 and 6 cases (33.5%) of prader 5 so we found that TUM technique is very beneficial in severely virilised 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. Jenak et al. 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. [16]

In our study, the anatomical and cosmetic outcomes, were 85% good,10% satisfactory and were poor in 5% of cases, While **Creighton et al** results were 18% good, 41% satisfactory and 41% poor. (5) **Gupta et al** results of 50 cases of feminizing genitoplasty, reported 74% As good, 20% as satisfactory and 6% as poor. [17] **Salle et al** reported that the genital appearance was considered good in 87.5% of cases and satisfactory in 12.5% of cases. Of the patients with good cosmesis 9.5% underwent subsequent minor reduction of the labia majora. [18]. While **Marei et al** results of 30 cases reported 73.3% as good, 20% as satisfactory and 6.6% as poor. [19]Our results lie close to both Marei et al and Salle et al. [18,19]but away from Creighton et al and those of Gupta

et al. [5,17]The last two studies were performed in 2001, 2006. Many improvements of the surgical understanding, equipment and accumulation of knowledge and skills must have certainly improved the outcomes. Vaginal stenosis is the most common complication after Vaginoplasty. [20]Before the use of TUM technique, there was a high incidence of vaginal stenosis of up to 78.5% and most patients required repeated surgeries. [21]A much lower incidence of vaginal stenosis was reported on using TUM, ranging from 0% [22]to 9.1%. [23] This is obviously because TUM decreased the incidence of vaginal ischemia. In our study, vaginal calibration was done easily in 19 cases (95%) using Hager dilators ranged from 7 to 15 mm and one case had vaginal stenosis that needed only dilatation regimen for 2 months with improvement.

Palmer et al defined continence as parental report of full toilet training with no accidents during the day and rare accidents (fewer than 2 per month) at night after the age of 3 years. In their review they had 91.7% continence after TUM and 100% after PUM, denoting no significant difference. [24]J. Stites et al had two cases of urinary incontinence following TUM out of 10 cases operated for CAH following vaginoplasty. [25]in our study, one case developed dysuria that was improved with medical treatment and one case developed stress incontinence after TUM.

Conclusion

Anatomic and cosmetic results after feminizing genital surgery at our institute showed an overall good outcome. Feminizing genitoplasty can be used safely and effectively to provide adequate introitus with excellent cosmetic appearance. The procedure can be done during infancy with good results provided that the surgeon is familiar with the procedure. The proper technique should be tailored to the severity of the anomaly so the decision to proceed from a PUM to a TUM is dependent upon the patient's anatomy. Adopting TUM approach has tremendously simplified the feminizing genitoplasty even in cases of high confluence of the vagina and urethera. Sigmoid vaginoplasty is a good choice in cases of CAH where the vaginal confluence was high close to the bladder neck and the vagina was very short.

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