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Original article

A study for Early Results and Complications of Feminizing Genitoplasty in Children Welfare Teaching Hospital, Medical City

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Abstract:

- ***Background*:** Differences of sexual development (DSD) is a congenital condition in which the development of the infant/child's chromosomal, gonadal, and anatomic sex are atypical. The aim of the study is to evaluate early results and complications of feminizing genitoplasty and to establish proper database for future research.
- ***Methods:*** A prospective descriptive study focused on 24 patients who underwent feminizing genitoplasty by the same pediatric surgery team. Operations included cutback vaginoplasty, partial urogenital mobilization, Fortunoff flap, or staged feminizing genitoplasty. Postoperatively, patients received IV analgesia and antibiotics throughout their hospital stay. Wound care began on the second day after surgery, involving normal saline and moist exposed burn ointment (MEBO).
- ***Result:*** The study included 24 patients aged 1 to 13 years (mean age: 6 years). Birth-assigned gender was 62.5% female and 37.5% male. Diagnoses comprised 95.83% CAH and 4.16% Partial Androgen Insensitivity Syndrome. Chromosomal analysis revealed 95.83% XX and 4.16% XY. Prader's classification indicated 74.07% as Prader3/4. Urogenital sinus length was ≤3cm in 83.33%, >3cm in 16.66%. Surgical approaches: 70.83% underwent partial urogenital mobilization with clitoroplasty, monsplasty, labioplasty, Fortunoff flap; 16.66% cutback vaginoplasty; 12.5% staged repair without vaginal replacement. Post-op, 8.33% experienced minor bleeding, 4.14% seroma, 16.66% wound infection, 4.16% minor labia majora wound dehiscence: no clitoral loss, urinary issues. Patient/family satisfaction: 87.5% reported good, 12.5% satisfactory outcomes.
- ***Conclusions:*** Feminizing genitoplasty is a safe surgery with relatively low complication rates and good cosmetic outcome when performed by surgeons with experience in this field.
- **Keywords:** Sex development disorders, congenital adrenal hyperplesia, feminizing genitoplasty, urogenital sinus mobilization, Fortunoff flap.

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INTRODUCTION

Differences of sexual development (DSD) is a congenital condition in which the development of the infant/child's chromosomal, gonadal, and anatomic sex are atypical. [1] The commonest is persistent urogenital sinus and virilization due to congenital adrenal hyperplasia (CAH) accounting for about 70%. [2] The incidence of true ambiguous genitalia is approximately 1:4500–5000.

Classification

A new classification released by the International Consensus Conference
on Intersex has largely replaced old classifications. This classification system breaks down DSDs into three broad categories: sex chromosomeDSDs, 46XY DSDs, and 46XX DSDs [3,4]

46XX DSD

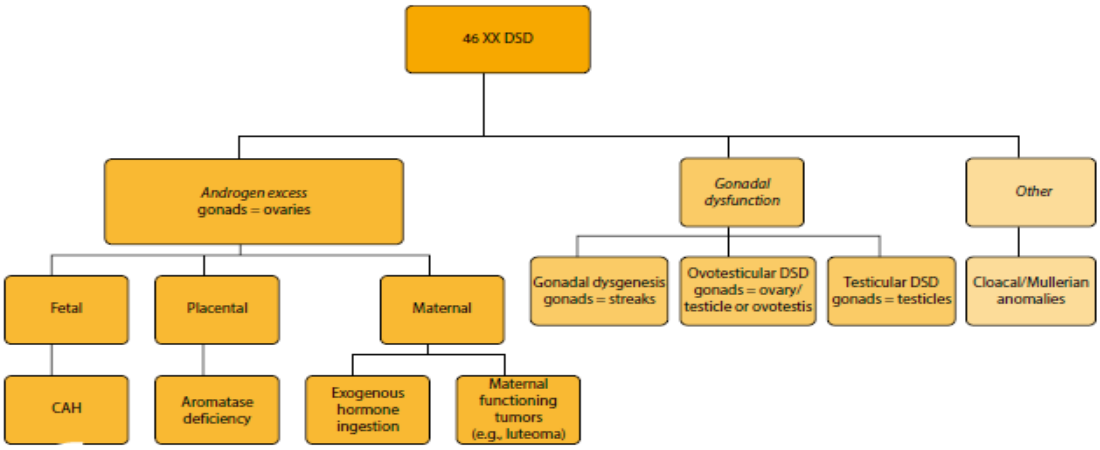

Figure 1. Different causes of 46XX DSD [5]

Congenital Adrenal Hyperplasia (CAH)

CAH happens with an incidence of 1:10,000 to 1:20,000, live births. [6] The genetic sex is female and the internal gonads are ovaries, while the external genitalia are virilized to resemble male features.[2] The vagina and urethra open into urogenital sinus rather than separately on the perineum.[7] About 75% of the patients will have salt-wasting CAH, which can present with a life-threatening salt-losing crisis in the first or second week of life.[8] There are four types of CAH.

Gender Assignment

Regarding gender identity, the vast majority of patients with CAH (~95%) identify as female and gender assignment is generally female given the 46XX karyotype. [9]

46XY DSD

XY DSD is a more diverse and heterogeneous group than XX DSD. [10] gender assignment discordant to karyotype (i.e., female assignment) is prevalent in this group.

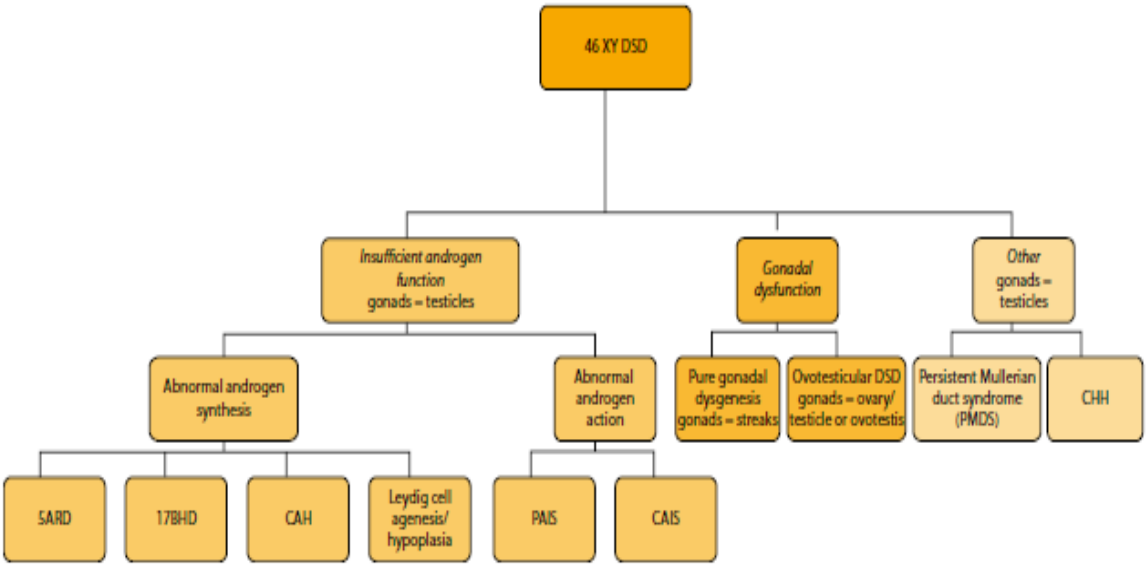

Figure 2 Diagram illustrating differential diagnoses for XY DSD. 5ARD, 5-alpha-reductase deficiency; 17BHD, 17-beta-hydroxysteroid dehydrogenase deficiency [(5)]

Disorders of Androgen Action

Partial Androgen Insensitivity Syndrome (PAIS)

Presents with variable degrees of undervirilization despite normal androgen production by the pituitary–gonadal axis, normal anti-Mullerian hormone and normal testicular histology. [(10)] gender assignment and treatment of (PAIS) are individualized. [(11)]

Complete Androgen Insensitivity Syndrome (CAIS)

Patients with CAIS do not present with genital ambiguity [(10)] Patients with CAIS are usually diagnosed in infancy or childhood when a testicle is palpated or found in the groin during an assessment or exploration for an inguinal hernia in an otherwise phenotypically normal female. Most CAIS patients are being raised as females at the time of diagnosis, so gender assignment is always female. [(12)] Classically, orchiectomy is recommended given the risk of malignant degeneration but is often deferred until after puberty. [(11)]

Persistent Mullerian Duct Syndrome

Persistent Mullerian duct syndrome (PMDS) does not present with genital ambiguity. Patients are usually males with cryptorchidism found to harbor Mullerian structures in the abdomen, [(5)] The most common presentation to the surgeon is that of finding a fallopian tube adjacent to an undescended testis in the hernia sac at the time of orchiopexy. [(13)]

SEX CHROMOSOME DSD (MOSAIC KARYOTYPE)

This subgroup includes any DSD patient with a mosaic karyotype. It encompasses patients with Turner (45 X) and Klinefelter syndromes. the main diagnosis in this group is mixed gonadal disgenesis MGD associated with a 45 X/46 XY karyotype. [(5)]

Mixed Gonadal Dysgenesis

Patients with MGD generally present with genital ambiguity, asymmetrical external genitalia, and not uncommonly, inguinal hernias. Their gonad configuration is streak or testicle. ([14])

The streak gonad is at risk for GB and should be removed irrespective of the sex of rearing. In patients raised as females, the testicle should be removed as well.

APPROACH TO THE NEWBORN WITH GENITAL AMBIGUITY

Newborns with genital ambiguity should be evaluated on an urgent basis for two reasons: to rule out congenital adrenal hyperplasia (CAH), since the salt-wasting form of the disease can be life threatening, and to provide a male or female gender assignment after a thorough, timely investigation. The first step is to request an evaluation by an expert in DSDs, who works as part of a multidisciplinary team. [(15)]

Detailed History and Physical Examination

Physical examination should initially focus on general findings and poten-tially life-threatening problems, like the presence of severe dehydration that can be associated with salt-wasting CAH. Examination of the genital tubercle and position and patency of the anus. Asymmetry is also an important sign to look for. [(16)] The urogenital sinus UGS represents a common channel of variable length for the urinary and genital tracts. The terms *low* (closer to the perineum) and *high* (closer to the bladder neck) are used to describe the level of the confluence between the urethra and vagina. Traditionally, the Prader classification has been widely used in an attempt to standardize such findings [(5)]

Diagnostic Tests

The most important initial diagnostic tests in the DSD workup are karyotype, pelvic ultrasound to evaluate the presence of Mullerian structures, and serum levels of sodium, potassium, and 17-hydroxyprogesterone (17OHP) after day 3 of life [(17)]

Pathology reports from gonadal biopsies or removal may be helpful in formulating a more complete diagnosis. [(5)] A genitogram helpful in identifying the level of confluence of a vagina and urethra and its relation to the urethral sphincter [(11)] Endoscopy is not usually required for diagnosis, but is essential in characterizing the internal duct structure, the level of confluence of the urogenital sinus, and planning for and performing the reconstructive procedures. [(18)]

Reconstructive Genital Surgical Procedures

The goals of gender assignment and management should include preservation of sexual function and any reproductive potential with the least number of operations, appropriate gender appearance with a stable gender identity, and psychosocial well-being. [(19)]

MALE GENDER ASSIGNMENT

Reconstructive efforts for the male gender of rearing include orchiopexy or orchiectomy, when appropriate, and hypospadias repair. [(20)]

FEMALE GENDER ASSIGNMENT

Feminizing genitoplasty includes: monsplasty, clitoroplasty, labioplasty and vaginoplasty. The timing of the vaginoplasty depends on the level of the confluence of the urogenital sinus. [(11)]

VAGINOPLASTY

The choice of technique for vaginoplasty is contingent on the site where the vagina opens into the UGS. Some reports have suggested that a common channel of ≤3 cm would be the cutoff between a high and a low vaginal opening. [(21)] Others have implied that the distance between the urethrovaginal confluence

and the bladder neck is in fact more important than the length of the common channel. [22]. From a surgical perspective, techniques range from flap vaginoplasties (Fortunoff and Passerini–Glazel) to vaginal pull-through after complete separation from the UGS, going through total and partial urogenital mobilization. [5] The Fortunoff flap was described in 1964 and consists of an inverted U-shaped incision in the perineum that is elevated as a flap and sutured to the posterior wall of the vagina. [5]

In the last two decades, total and partial urogenital sinus mobilization (TUM and PUM, respectively) have been introduced to the surgical armamentarium of vaginoplasties.[22] TUM seems to produce better results than flap vaginoplasties, especially in low UGS.[23] Nonetheless, the problem of high vagina remains, due to the need of extensive mobilization, which is conce-rning for the possibility of disrupting the urinary continence mechanism by placing undue traction on the bladder neck. To limit such potential disruption, PUM was devised, where the same principles of TUM are followed, except that the pubourethral ligaments are not incised. [24] In some patients with a high urogenital confluence, vaginal reconstruction is delayed until the peripubertal period. The techniques described are still used, but in some patients, especially those who are obese, these methods are insufficient. In such cases, vaginal substitution with a colonic segment is preferred [11], The of this study is to evalute early results and complications of Feminizing genitoplasty and to establish proper data base for future research.

MATERIALS and METHODS:

This is a prospective descriptive study (observational) conducted at children welfare teaching hospital, Baghdad medical city from the period of February 2019 to October 2021. Within this time there was a period of cessation of operations due to the peak of COVID-19 pandemic. The study included a total number of 24 patients

Inclusion criteria

Any patient under 14 years old who has ambiguous genitalia.

Exclusion criteria

Patient who needs male gender assignment

Preoperative evaluations

After taking full history and clinical examinations. The patients were sent for the endocrinologist to complete their assessment and management specially regarding CAH management and chromosomal study,after that complete blood count, renal function test, bleeding profile, virology screen, urinalysis, urine for culture and sensitivity, blood group, abdominal ultra-sound, and chest x-ray, as preoperative measures to proceed to surgery. The consent had been taken from the family. All of the operations done by the same surgical team. For all cases of CAH, the oral hydrocortisone was converted to I.V H.C the night before surgery and the morning of the surgery and kept on double dose post op for 3 days. All patients kept on antibiotics and analgesia post op during the length of hospital stay with local wound care after surgery by the surgical team.

Data collection and surgical procedure:

All patients were anesthetized by general anesthesia and all patients received peri-operative antibiotics at time of induction in the form of third gene-ration cephalosporin (ceftriaxone) or in case of allergy amikacin was given. Patients were put in liethiotomy position and panendoscopy was done for them

all to assess the presence and length of the urogenital sinus and insertion of foley's catheter to the urethra and the vagina(under guide of cystoscope if necessary) then circumcising incision done and degloving of the shaft then dissection done between the corpus spongiosum (within it the urethra) and corpus cavernosum separating them, then urogenital mobilization started (if needed) by dissecting the urogenital sinus as a single block and mobilizing it, then vaginoplasty done using inverted U shaped incisions (Fortunoff flap) and suturing the flap to the posterior wall of the vagina then subtunical dissection of the corporal bodies done preserving the neurovascular bundle and proximal bodies were controlled at the level of the crura by suture ligation (vicryl 0) and resection of the corporal bodies then clitoroplasty done either by glans reduction or without reduction accordingly and was preceded by a stitch to the periostium of the pubic bone using vicryl 4.0 then the penile shaft skin was incised longitudinall and was used to create the labia minora and the scrotal type skin was modified to create the labia majora suturing using vicryl 6.0 washing the wound with N.S then dressing done, in some cases with high confluence who needs vaginal replacement It was not done and deferred for another session ..and in some cases only cutback vaginoplasty was sufficient. operation time was 6 hours in mean. postoperatively patient kept on IV analgesia and antibiotics for the duration of hospital stay and wound care started at day 2 post op using normal saline and moist exposed burn ointment (MEBO) restriction of movement in the early post operative period, patient stayed in the hospital for a range of 5-12 days.

Statistical analysis

The collected data were amalysed using excel program. Descriptive statistics including frequencies and percentages of the data were presented in tables and graphics.

Ethical considerations

The research topic was approved by the supervising scientific council of the Iraqi Board of Pediatric Surgery-Iraqi Board of Medical Specialties and children Welfare teaching Hospital.

RESULTS

Age distribution:

A total of 24 patients were enrolled in this study with age ranging from 1 to 13 years with mean age of 6 years

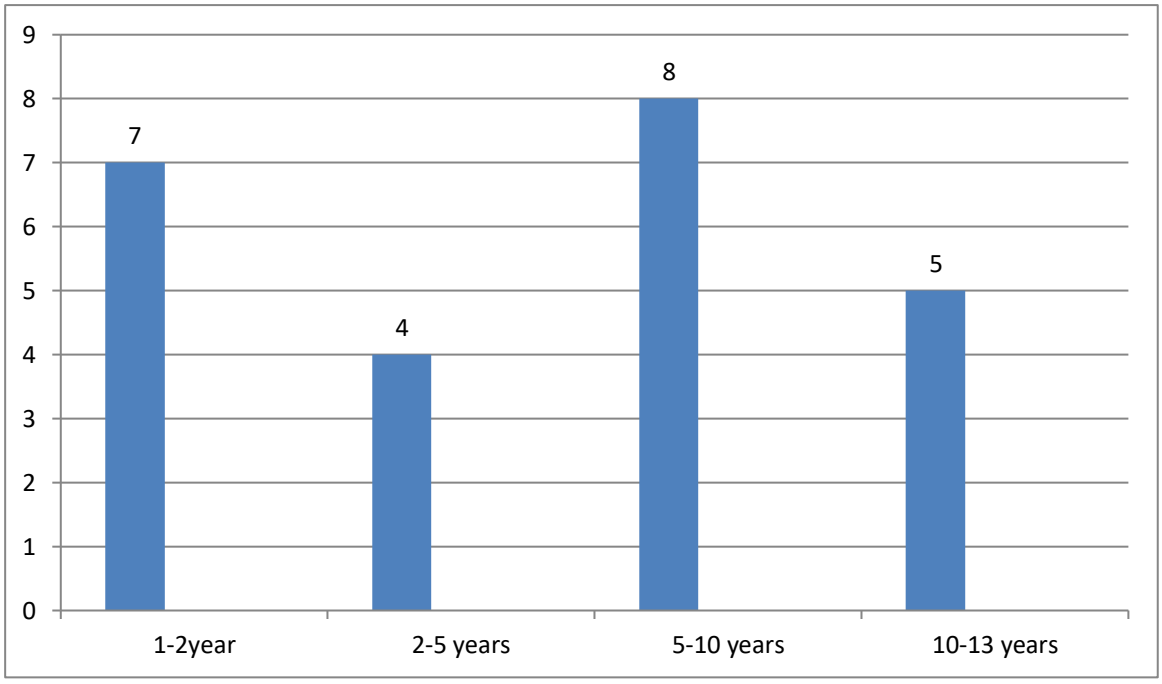

Figure 3. Age distribution

Most of the patients were aged between 5 – 10 years with percentage of 33.33%, patients with age 1-2 years 29.16 %, from 2-5 years 16.66 %, and 10-13 years 20.83 %.

Gender assigned at birth:

The gender assigned at birth was female in 15 (62.5%) patients while it was male in 9(37.5%) of patients.

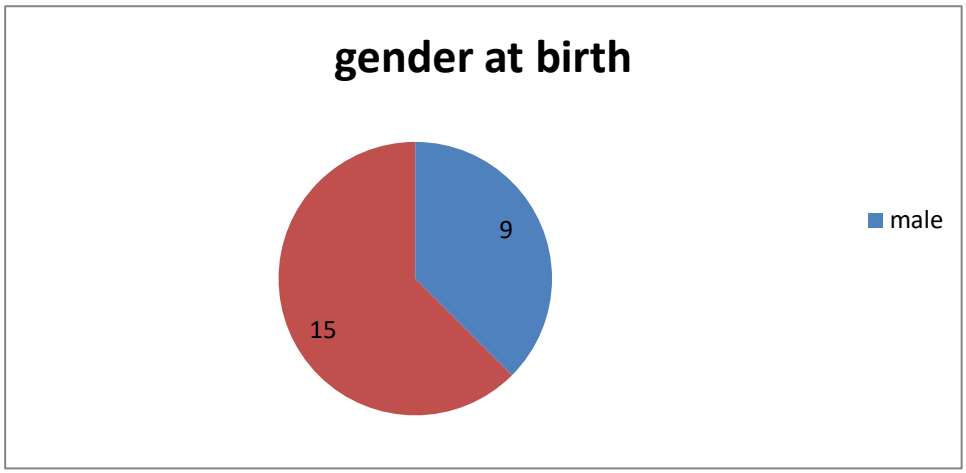

Figure 4. gender assigned at birth.

The diagnosis

Regarding the diagnosis, CAH were seen in most patients 23 (95.83%), while PAIS was found in 1 (4.16%).

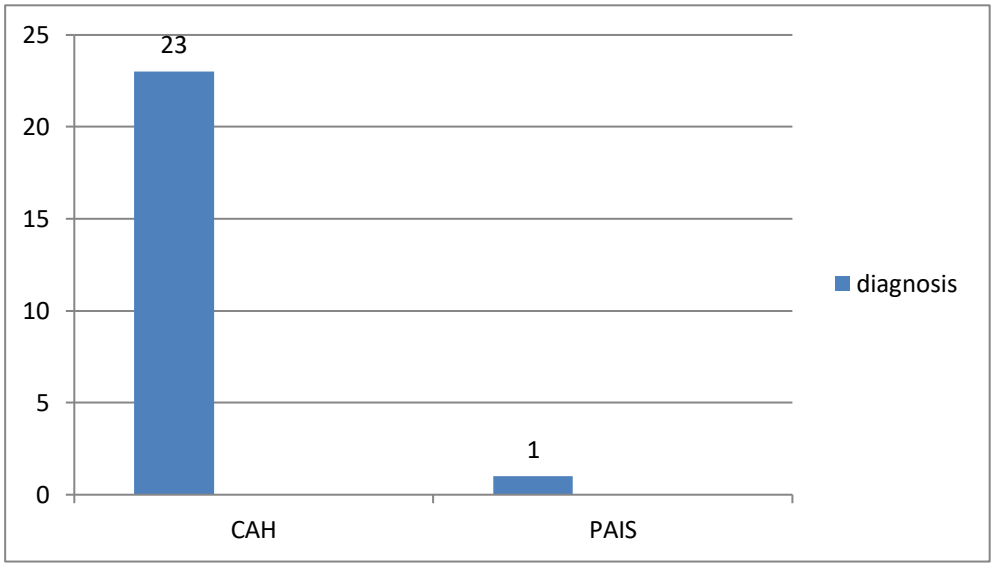

Figure 5. The distribution of studied cases according to the diagnosis of CAH

The chromosomal study was XX in 23(95.83%) of patients and XY in 1(4.16%) of patients.

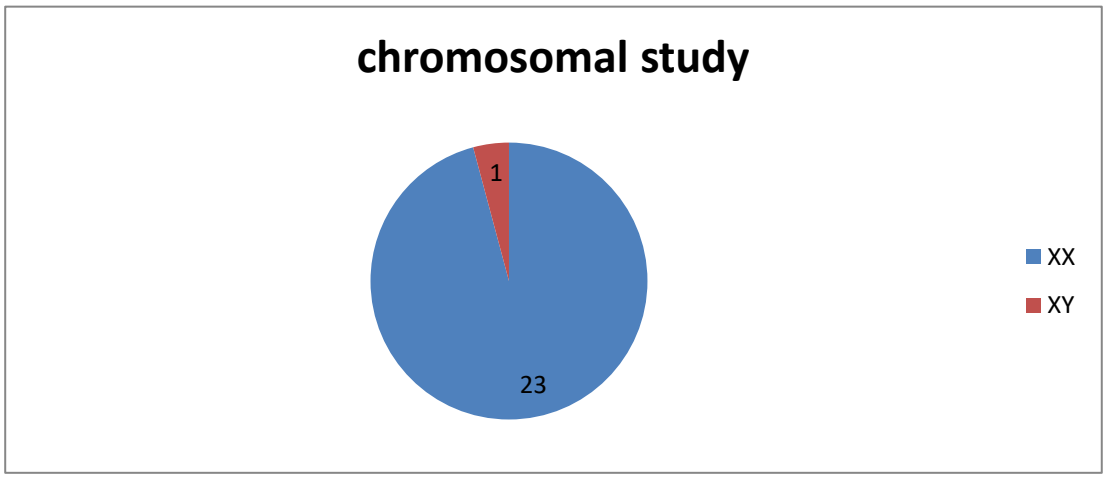

Figure 6. Chromosomal study

Prader classification

regarding Prader's classification 1 (4.16%) patients was Prader 1, 5(20.83%) patients were Prader 2, 7(29.16%) patients were Prader 3, 10(41.66%) patients were Prader 4, and 1(4.16%) patient was Prader 5.

Table 1 Prader classification

Prader classification	Number	Percentage
Prader 1	1	4.16%
Prader 2	5	20.83%
Prader 3	7	29.16%
Prader 4	10	41.66%
Prader 5	1	4.16%
Total	24	100%

Length of UGS

The length of the urogenital sinus was ≤ 3cm in 20 (83.33%) of patients and > 3 cm in 4 (16.66%) of patients

Table 2 length of urogenital sinus

Urogenital sinus length	Number	Percentage
≤ 3 cm	20	83.33%
> 3 cm	4	16.66%
Total	24	100%

Type of surgery

In regards to the technique and type of surgery, Partial urogenital mobilization (PUM) with clitoroplasty, monsplasty, labioplasty and Fortunoff flap (F) was done in 17(70.83%) , clitoroplasty, labioplasty with monsplasty and cutback vaginoplasty in 4 (16.66%), and staged repair with clitoroplasy monsplasty and labioplasty without vaginal replacement in 3(12.5%) of the patients.

Table 3 type of surgery

Type of surgery	Number	Percentage
PUM+F	17	70.83%
Cutback vaginoplasty	4	16.66%
Staged repair	3	12.5%
Total	24	100%

Early postoperative complications

Regarding early post operative complications it was categorized according to the table below 2 (8.33%) patient had minor bleeding,1 (4.14%)patient had seroma, 4(16.66%) of patients had superficial wound infection managed with wound care, 1 (4.16%) patient had minor wound dehiscence of labia majora managed with wound care alone, and none of the patients had clitoral loss

Table 4 early post operative complications

Complications	Number `	Percentage
Minor Bleeding	1	4.16%
Haematoma/seroma	1	4.16%
Wound infection	4	16.66%
Wound dehesince	1	4.16%
Clitoral loss	0	0 %

In regard to urinary control in the early post operative period, no cases of urinary incontinence or urine retention were found in the patients who were previously continent

Patient and family satisfaction

Patient and family satisfaction regarding the results of the feminzing genitoplasty were surveyed and were categorized in the table below.

Table 5 Patient and Family satisfaction

Patient and family satisfaction	Number	Percentage
Good	21	87.5%
Satisfactory	3	12.5%
Poor	0	0%
Total	24	100%

DISCUSSION

DSD is a stressful condition to the family and one of the most challenging cases to face a pediatric surgeon/pediatric urologist and require a multidisciplinary team including pediatric urologist/surgeon, endocrinologist geneticist, neonatologist, psychologist. [5]

This study is designed to be a baseline data for feminizing genitoplasy.

the mean age for performing the feminizing genitoplasy in our study was 6 years which is comparable with Akbiyik F et al [25] in which mean age of surgery was 4 years and differs from AbouZeid A et al [26] and Kudela G et al [27] with mean age of 2.5 years and 1.5 years respectively this difference is probably due to late presentation because of the social stigma of the ambiguous genitalia.

The sex assigned at birth was female in (62.5%) paitents while it was male (37.5%) of patients this high percentage of male gender assignment which was later on re-assigned as female before or after the surgery was mostly because of lack of multidisciplinary team approach at birth for ambiguous genitalia neonates to assign the appropriate sex for them after completing the required investigations to reach the diagnosis which could take weeks.

The diagnosis was CAH (95.83%) patients which is similar to Akbiyik F et al [25] in which CAH was the primary diagnosis in (97.56%) and Baskin A et al [28] in which CAH was found in (91%) and differs

from Bocciardi A et al[29] were CAH was found in (62.35%) this difference in the percentage is probably due to larger sample of cases in the latter study.

regarding Prader's classification the majority of cases were prader 3 and 4 (70.83%) which is comparable to Sircili MH et al[30] and Baskin A et al[28]

were prader 3 and 4 percentage were (74.07%) and (88%) respectively and also to Marei M et al[1] where it was (76.7%).

In regards to the length of the urogenital sinus length it was <= 3cm(low) in (83.33%) of patients and > 3 cm (high) in(16.66%) of patients which differs from Kudela G et al[27] in which low confluence was (61.26%) and high confluence was found in (38.70%) this difference can be explained by the larger sample size in Kudela G et al and the margin of error that can happen during the objective measuring of the UGS length which is an important determinant of the type of feminizing genitoplasty done for the patient .

The type of feminizing genitoplasty was mainly PUM with Fortunoff flap in (70.83%) which is comparable to Marei M et al[2] in which PUM was used in (76.7%) and it differs from Palmer BW et al[31] in which PUM was used in only (28%) and Badawy H et al[32] in which PUM was used in (26%) this difference can be explained by the fact that badawy et al mainly concentrated on single stage feminizing genitoplasty which necessitates TUM for long confluence and the fact that the risk of urinary incontinence which comes with TUM was mainly unacceptable by the guardians of our patients.

Early post operative complications

minor bleeding occurred in 4.16% of patient that just required pressure dressing, which is comparable to Sircili MH et al[30] were minor bleeding percentage was 5.88% and higher than Bernabé KJ et al[33] who reported no cases of post operative bleeding this low rate of bleeding in such vascular area can be explained by good intra operative hemostasis using bipolar cautery and pressure dressing post operatively with restriction of movement in the early post operative period .

seroma with notable swelling occurred in 4.16% of patients which resolved by manual evacuation and no further action required which is comparable to Badawy H et al[32] where seroma/haematoma occurred in 3.33% of cases.

wound infection occurred with 16.66% of cases which was managed with wound care alone..this perentage was higher than Badawy H et al[32], Bernabé KJ et al[33] and Farkas A et al[34] in which percentage of wound infection were 3.33%, zero, and 2% respectively which mostly indicates the need for better infection control in the operating room or in the ward post operatively.

There was no incidence of clitoral loss in our study which is the same in Bernabé KJ et al[33] while Sircili MH et al[30] reported a 2.9 % of glans necrosis and loss, Badawy H et al[32] also reported a 3.33% of clitoral loss and in Farkas A et al[34] it was 2%.. this could be because of the smaller sample in our study, the meticulous dissection, and the technique used during the surgery where magnification loupe was used in all the surgeries to avoid injury to the neurovascular bundle while it's not mentioned in these studies whether magnification was used or not.

In regard to urinary control no one had complained from urine incontinence in the early post operative period in those patients who were continent preoperatively this is similarly seen in Palmer BW et al[31] while in Badawy H et al[32] stress urinary incontinence persisted for 6 months was noted in 20% of the

patients this good result regarding continuance is probably because of the use of PUM mainly in our study. Regarding patient and family satisfaction 87.5% of them reported good results, this is similar to Braga LH et al [35] where the good results were also (87.5%) and is comparable to Marei M et al [2] with (73.3%) reporting good results and is higher than Sircili MH et al [30] where good results were at percentage of (68%).

CONCLUSION:

We concluded that feminizing genitoplasty is a safe surgery with relatively low complication rates and good cosmetic results when performed by surgical team with experience in this field.

There are many techniques for feminizing genitoplasty , The proper technique should be tailored to the severity of the anomaly and the length of the UGS.

UGS mobilization is a valuable maneuver in feminizing surgery in many aspects. It solves technical problems and facilitates dissection, maintains adequate blood supply to the urethra and vagina, and has good cosmetic outcome with low incidence of complications and without affecting mechanisms of urinary continence.

Recommendations

- we recommend the early multidisciplinary team approach for patient with ambiguous genitalia to help reach early diagnosis and provide education to the family and manage the family concern and early referral of the cases to tertiary centers.
- to perform a study for larger number of cases and for longer durations to determine the long term complications and address the psychosexual aspects. We should work on better sterilization of the operation rooms the surgical instruments, the surgical wards to decrease the risk of post operative wound infection.

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Nil.

Conflicts of interest:

There are no conflicts of interest**.**

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