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Original Article

Gender Identity and Assignment Recommendations in Disorders of Sex Development (DSD) Patients: 20 years' Experience and Challenges

Gurbuz F et al. Gender Identity and Assignment

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What is already known on this topic?
Gender assignment in Disorders of Sex Development (DSD) patients is always very difficult, complex and demanding experience in the management for both families and clinicians, particularly in cases where the gender appropriate for the clinical diagnosis is incompatible with the psychological gender of the patient. Gender assignment councils must have an experienced and multidisciplinary approach.

What this study adds?
Here, we present 20 years of experience and challenges in gender assignment, the causes and clinical characteristics of patients with DSD. This study is the longest timeframe, is the most comprehensive and has the largest number of cases in terms of gender assignment recommendation and assessing the factors affecting gender assignment from Turkey.

Abstract

BACKGROUND:
Gender assignment in infants and children with disorders of sex development (DSD) is a stressful situation for both patient/families and medical professionals.

METHODS:
The purpose of this study was to investigate the results of gender assignment recommendations in children with DSD in our clinic from 1999 through 2019.

RESULTS:
The mean age of the 226 patients with DSD at the time of first admission were 3.05 ±4.70 years. 50.9% of patients were 46,XY DSD, 42.9% were 46,XX DSD and 6.2% were sex chromosome DSD. Congenital adrenal hyperplasia (majority of patients had 21-OH deficiency) was the most common etiological cause of 46,XX DSD. In 46,XX patients, 87 of 99 (89.7%) were recommended to be raised as a female, 6 as a male, and 4 were followed up. In 46,XY patients, 40 of 115 (34.8%) were recommended to be raised as a female, and 70 as male (60.9%). In sex chromosome DSD patients, 3 of 14 were recommended to be raised as a female, 9 as a male. The greatest difficulty in making gender assignment recommendations were in the 46 XY DSD group.

CONCLUSION:
We present 20 years of experience in DSD gender assignment recommendations, and find that the etiologic diagnosis, psychiatric gender orientation, expectation of the family, phallus length and Prader stage were effective in the gender assignment in DSD cases (especially the first two factors). It is important to share these experiences among the medical professionals who are routinely charged with this difficult task in multidisciplinary councils.

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Introduction

According to the Jost's paradigm, the first sexual development stage begins with the identification of the chromosomal sex at the time of fertilization and completed as a result of many biological process (1). Money et al. (2) added the theory of psychosexual development to this paradigm. This theory is influenced by hormonal and genetic status, environmental and psychosocial experiences, social and parent's behaviors (3-5). Any defect occurring during this complicated process of sexual

differentiation may lead to a discordant development of chromosomal, gonadal, anatomical sex/phenotype and is defined as Disorders of Sex Development (DSD) (6-8). DSD are a heterogeneous group of rare situations which include various etiologies and presentations (9-11). The incidence of DSD is almost 1 in 4,500–5,500 (10-12).
The long-term physical, social and psychological outcomes of patients with DSD are still unclear. There are increasing concerns regarding early decisions about gender assignment in recent reports (13-18). Studies were generally conducted on psychosexual and surgical outcomes of this group of patients (19-22). Gender assignment of a child with DSD is the most difficult and stressful condition for both the family and the clinician, especially in cases of ambiguous genitalia (6, 23, 24). The families always want to know the actual gender of their DSD babies as soon as possible and give their babies a gender appropriate name. The primary goal in DSD is for gender identity to be consistent with the gender assigned (6). In this respect, a multidisciplinary approach is required for the diagnosis and treatment of DSD (25). Influencing factors to consider when debating gender assignment include medical diagnosis, external genital appearance, potential of fertility and sexuality, therapeutic and/or surgical intervention options, views and desires of the patients and their families, sociocultural factors, and the psychological gender development status of child (26-28).
There is a multidisciplinary council to make gender assignment recommendations in DSD patients, which consists of pediatric endocrinology, pediatric surgery, pediatric psychiatry, medical genetics and forensic science specialists in our clinic. Here, we presented our 20 years of experience of assistance with gender assignment in DSD patients as the single center in the region.

Materials and Methods

The purpose of this study was to investigate the results of gender assignment recommendations in children with DSD and the factors affecting these results in our clinic. In the present study, the file records of the 226 children with DSD admitted to the Department of Pediatric Endocrinology of Cukurova University between the years of 1999 and 2019 were reviewed. The clinical diagnosis of a DSD was supported by anatomical examination findings, gonadal and pelvic ultrasound, cytogenetic studies, determination of serum electrolytes, 17-hydroxyprogesterone levels, the ratio of testosterone-dihydrotestosterone (basal and hCG stimulated), and molecular genetic testing. 21-Hydroxilase Deficiency (72 of 88), 11-beta-hydroxylase deficiency (6 of 6), 17-beta-hydroxysteroid dehydrogenase type 3 deficiency (4 of 4) , Steroidogenic Acute Regulatory Protein gene mutations (5 of 5), complete androgen resistance (8 of 9), incomplete androgen resistance (6 of 6), 5-alpha-reductase deficiency, (19 of 19), Leydig cell aplasia/hypoplasia (2 of 2), 17-alpha-hydroxylase deficiency, (1 of 1), DAX1(NR0B1) (2 of 2), NR5A1 (SF1) (2 of 2) , Persistent Mullerian Duct Syndrome (1 of 1), Klinefelter syndrome (2 of 2) diagnosed by cytogenetic studies and molecular genetic analyses. mix gonadal dysgenesis, gonadal dysgenesis, ovotestis, Sertoli cell only syndrome diagnosed by especially laparoscopy with gonadal biopsy, and molecular genetic testing. All the genetic testing had been performed for diagnosis purpose after the approval of consent form from the patients and child's legal representative.
Laparoscopy and gonadal biopsy were performed in selected DSD patients for determination of gonadal histology. Cystoscopy was performed in order to examine urethra, uterus and uterine remnants.
Our center is the only one, and the oldest and largest 'Gender Evaluation Council' of our region. This council consists of pediatric endocrinologists, pediatric surgeons, child psychiatrists, specialists in forensic medicine and a medical geneticist. Gender assignments were recommended by this council. The role of the council is to evaluate medical data, to discuss among experts, and to provide information and medical advice to the patient and/or family. The council ensures that ample time and opportunities are provided to patient and families for their questions, concerns, and counseling needs.
Exclusion criteria for this study was these: DSD patients who did not need gender assignment (therefore not discussed in the council) such as Turner syndrome and isolated hypospadias. Written inform consent was obtained after the council from the parents or legal guardians of all the patients before participation. The study protocol was approved by the Ethics Committee of Cukurova University and performed in accordance with the ethical standards of the declaration of Helsinki (ethical decision no: 452018.77/10).
Background clinical data obtained from medical file records included age at the time of first admission and meeting, reason for admission, genital examination findings, Prader stage, karyotype, diagnosis, psychiatric gender orientations, gender patient is raised as, parents' views and requests for the gender, council meeting numbers, and gender assigned. Although genital phenotype evaluation according to the Sinnecker classification is more appropriate for 46,XY DSD cases (29), all patients were evaluated via Prader classification in order to avoid confusion (30).
The patients were classified into three main groups on the basis of the karyotype of the affected individual, according to The Lawson Wilkins Pediatric Endocrine Society (LWPES) and the European Society for Paediatric Endocrinology (ESPE) consensus (8, 9, 31). These groups are; 46,XX DSD, 46,XY DSD and Sex chromosome DSD.
The psychological evaluation for gender orientation was based on psychiatric interview with children and according to Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) diagnostic criteria (32).

Statistical Analysis

All analyses were performed using IBM SPSS Statistics Version 20.0 statistical software package. Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation. Chi-square test was used to compare categorical variables between the groups. The normality of distribution for continuous variables was confirmed with the Shapiro Wilk test. For comparison of continuous variables between two groups, the Student's t-test or Mann-Whitney U test was used depending on whether the statistical hypotheses were fulfilled or not. For comparison of continuous variables between more than two groups, Kruskal Wallis test was used. The statistical level of significance for all tests was considered to be 0.05.

Results

A total of 226 patients were classified with 46,XY DSD (n:115, 50.9%), 46,XX DSD (n:97, 42.9%) and sex chromosome DSD (n:14, 6.2%) (Table 1). The mean age at first admission of the patients was 3.05 ±4.70 (min:0-max:17.58) years.
Of the 226 patients, ambiguous genitalia (n:141, 62.4%) were the most frequency cause of admission for all 3 groups (Table 1).

When the diagnostic distribution of the patients was examined, congenital adrenal hyperplasia (CAH) was in the most common cause of DSD. Among the 46,XX DSD (n:97) patients, 21-Hydroxilase Deficiency (21-OHD) was the most diagnosed (n:88, 90.7%) (Table 1). The main cause in 46,XY DSD cases (n:115) was 5-alpha reductase deficiency (n:19, 16.5%). This was followed by complete (CAIS) and incomplete androgen resistance (PAIS). Forty-two (18.6%) of all cases had undetermined causes for DSD. The vast majority of these were 46,XY DSD cases (40/42) (Table 1,2).
The psychiatric evaluation of cases; only about half of the 46,XX DSD patients had female, one in three 46,XY DSD patients had male gender orientation. In the sex chromosome DSD cases, female gender was 4 and male gender was 5 of 14 patients (Figure 1).
The mean age of all cases was 4.46 ± 4.98 years (min: 0.12-max: 18.63) at the time of the council meeting. (46, XX DSD, 46, XY DSD and Sex chromosome DSD patients were 3.20 ± 3.92 years, 5.49 ± 5.41 years and 4.77 ± 6.15 years, respectively, p=0.004). While 200 (88.5%) of 226 patients had gender assignment in the first council meeting, 26 patients (11.5%) had more than one council meetings (18/26 were 46, XY DSD, 6 were 46,XX DSD and 2 were sex chromosomal DSD patients). Especially, patients who were found to have more than one meeting were 46,XY DSD cases.
In 46,XY DSD patients, 40 of 115 (34.8%) were recommended to be assigned as a female gender (Figure 1). The female gender assignment recommendation in these cases was made for all of the complete androgen resistance, Leydig cell aplasia/hypoplasia, Steroidogenic Acute Regulatory Protein (STAR) gene mutations, 17-alpha hydroxylase and DAX1 (DSS-AHC Region on Human X Chromosome, NR0B1) mutation cases according to the genetic diagnosis (Table 2).
Eleven of 226 cases (4.8%) were followed without a gender assignment (Figure 1). The common characteristics of all these cases who were decided to follow up were chromosomal analysis, specific diagnosis, Prader stage and psychiatric evaluation were incompatible with the family's gender expectation.
While the effect of the phallus length on the assignment recommendation was examined, it was found that in all three groups, the phallus length was significantly higher in males than in the females (Table 3).
According to the Prader classification with gender assignments recommendation, lower Prader stages (especially stage 1) were effective in making a female gender assignment in 46, XY DSD and sex chromosomal DSD cases. In addition, as the Prader stage increased, the decision-making ratio was gradually increased in favor of the male gender. However, the higher Prader stages were not effective in making a male gender assignment in 46,XX DSD cases. Moreover, the gender assignment of patients with Prader stage 1-4 was the female gender in a very large number of the 46,XX DSD cases. In general, it was found that a lower Prader stage was more effective in making a female gender assignment recommendation, than making a male gender assignment recommendation with a higher Prader stage (Table 4).

Discussion

In this study, we present 20 years of experience in helping gender assignment, the causes and clinical characteristics of patients with DSD in our clinic. Gender assignment is always very difficult, complex and demanding experience in the management of patients with DSD for both families and clinicians, particularly in cases where the gender appropriate for the clinical diagnosis is incompatible with the psychological gender of the patient. It should be recognized that every DSD is unique and has to be treated with individualized care. To our knowledge, this study has the longest timeframe, is the most comprehensive and has the largest number of cases in terms of gender assignment recommendation and assessing the factors affecting gender assignment from Turkey.
DSD are a heterogeneous group of conditions which has an estimated incidence of 1:4500-5500 (10-12, 33, 34). In a recent study from Turkey by Aydin et al. (35), it was found that the DSD newborn with ambiguous genitalia rate was among 1.3/1000 newborns. However, this rate may be more common in our region where we have an increase in autosomal recessive forms of DSD due to higher rates of consanguinity, around 20% to 25% (35). Because the consanguineous marriage rate that Aydin et al. (35) specified did not seem to be very high. Nordenvall et al. (36) remarked that the developmental anomalies of the external genitalia may be seen in 1:300 infants. But, not all of these conditions often need gender assignment, such as isolated undescended testis and/or hypospadias.
The previous studies have reported that 46,XY DSD patients had higher incidence than other DSD patients (35, 37-42). In our study, we also found that the most common patients were 46,XY DSD (50.9%) in accordance with the literature. In a study with 117 patients from Thailand, they reported that most of the cases were sex chromosome DSD (%53) (43). However, the majority of these patients were Turner syndrome. We did not include patients with turner syndrome in our study because of no have an ambiguous genitalia status to needs gender assignment. We only included two Klinefelter syndrome patients because of the ambiguous genitalia complaint and we did not incorporate any other Klinefelter syndrome patients.
Most of the patients with DSD are referred with ambiguous genitalia (35, 37-39, 43)**.** In this study, ambiguous genitalia were the most common cause of admissions for all three DSD classifications (Table 1).
Despite the current advanced genetic analyses, a definitive genetic diagnosis can only be made in about 20% of cases of DSD (11, 12, 31, 37). Compatible with this information, the rate of patients with undetermined causes of DSD was 18.6% (n: 42 of 226) in our study. There were only two patients (2%) with undetermined causes in 46,XX DSD group. The majority of undiagnosed patients were 46,XY DSD cases (n: 40 of 115, 34.7%).
The etiologic cause of most of the patients with 46,XX DSD is CAH due to 21-OHD (37-39, 44). In this study, CAH was the most common underlying etiological condition of 46,XX DSD (Table 1). CAH due to 21-OHD and 11-OHD accounted for 97.9% of 46,XX DSD in our series. Similarly, Ocal et al. (39) from Turkey found that, 21-OHD and 11-OHD were the most frequency (88.8%) etiology of their 46,XX DSD group. Again, De Paula et al. (38) from Brazil with a 408 case series of genital ambiguity, Al-Muttair et al. (45) from Saudi Arabia with a total of 120 DSD patients, and Al-Agha et al. (46) report that the main etiology of 46,XX DSD was 21-OHD. But, Ganie et al. (37) specified that the main referring cause of 46,XX DSD was ovotesticular.
In 46 XY DSD cases, only 50% of patients can be diagnosed with a definite diagnosis (44). In our study, the rate of 46,XY DSD patients with diagnosed causes was higher (n:75, 65.2%). 5-alpha reductase deficiency was the first, CAIS and PAIS were also the second main etiologic causes of 46,XY DSD (Table 1,2). The etiological distributions of both our 46,XX DSD

and 46,XY DSD patients were similar to previous studies (38, 39, 41, 45-47). Contrary to this, Ganie et al. (37) report that the main etiological cause of 46,XY DSD was disorder of androgen synthesis or action.
Mix gonadal dysgenesis had the largest share of etiologic cause of sex chromosome DSD group in our study (85.7%). Jaruratanasirikul et al. (43) from Thailand reported that the most common sex chromosome DSD was Turner syndrome. Similar to this report, Ganie et al. (37) from South Africa, with total 346 cases diagnosed with DSD, noted that Turner syndrome had the biggest share for sex chromosome DSD etiology (61%).
Gender identity is a process which is influenced by various prenatal and postnatal variables. Psychosexual development plays an important role in the formation of sexual identity. And this condition is the main structure of sexual identity, and it is influenced by genetic status, pre/postnatal exposure to androgens, sociocultural factors, and family dynamics (6, 39, 48, 49). Gender assignment is an important problem in DSD patients who have virilized brain with undervirilized external genitalia (13-15, 39).
Eleven of 97 46,XX patients (11.3%) had male gender orientation in the psychological evaluation, and raised as male gender by parents (9 were 21-OHD, 1 was 11-OHD, and 1 was Sertoli cell only syndrome, mean age of cases was 9.92 ± 4.96 years). At the council meeting, 6 of these 11cases were gender assignment recommendation as male, 2 as female and 3 were recommended to be followed up.
Five of the patients who received a male assignment recommendation were 46,XX 21-OHD CAH, other one was Sertoli cell only syndrome (Table 2). The mean age at presentation and at the time of the meeting of these five 21-OHD CAH patients was 7.56 ± 5.26 years and 10.66 ± 3.88 years, respectively. It was found that all of these patients were Prader stage 4-5, raised as male and their psychologic gender orientation was male, and all of the parents demanded a male gender assignment. For the determinative factors to recommend gender assignment in 46,XX cases; besides the etiological diagnosis, age, psychologic gender and Prader staging were showed us how important for assignment decisions (Table 2,4).
Similar to our study, Khattab et al. (13) report three 46,XX with 21-OHD CAH patients who reared as male gender. In another study, of the 50 DSD patients, the 4/11 cases diagnosed with 46,XX DSD due to CAH had assumed male gender role (15). This condition occurs due to prenatal and/or postnatal exposure to high levels of androgens that promote the masculinization of gender behaviors (16, 50). With recent implementation of national neonatal CAH screening, we hope that late diagnosis of CAH, therefore ambiguous genitalia will be prevented.
For our council, the greatest difficulty in making gender assignment recommendations were in the 46 XY DSD group. The mean length of the phallus of patients who received a female assignment was 0.82 ± 0.71 cm and 90% were Prader stage 1-2 (etiological causes of these cases were given in Table 2).
Most of the 46,XY DSD patients who had no etiological diagnosis and had female gender assignment recommendations were Prader stage 1-2 (according to psychological evaluation for these cases, 8/9 had female gender, and 1/9 had no gender orientation).
93.7% of the 46,XY cases with a male gender assignment recommendation and no etiological diagnosis were Prader stage 3-5. Moreover, 62.5% of these patients had no gender orientation yet. With these findings, we inferred that besides the etiologic diagnosis, expectation of the family, phallus length and Prader stage were effective in the female assignment recommendations in 46,XY DSD cases. Furthermore, if there is no definite etiologic diagnosis, the most important factors in determining the gender assignment recommendation in 46, XY DSD patients were Prader stage and psychological gender orientation.

Study Limitations

The major limitation of this study was only covered the period of the gender assignment recommendation council. Due to ethical concerns, follow-up of patients after gender assignment recommendations were not included in study.

Conclusion

In conclusion, the most difficult condition in a patient with DSD diagnosis who has ambiguous genitalia is the assignment of an appropriate gender. Specific diagnosis and psychological gender are more effective in gender assignment of DSD patients with an etiologic cause. Phallus length and Prader stage are important criteria in the gender assignment of patients with undiagnosed DSD. In fact, in this study, it was found that none of the features of the patients dominated the gender assignment alone. Gender assignment should be determined by evaluating the patient's chromosome structure, specific diagnosis, fertility, Prader stage, phallus length, psychological orientation, family wish and the opinion of experienced a council of specialist physicians. Gender assignment becomes more difficult especially if there is a mismatch of the gender the child is raised as, with the etiologic diagnosis. The most important experience of our council over the years is that the decision should be left to the patient with avoiding irreversible surgical procedures up to age 18. Gender assignment council of centers must have an experienced and multidisciplinary approach to the diagnosis, medical and/or surgical treatment, psychosocial support, and genetic counseling of patients with DSD. Providing the centers' experiences in the field of gender assignment in DSD patients to the literature will be beneficial for other patients in the decision-making process.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

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Table 1. Distribution of admission reasons and etiological causes of patients

		Reason for admission									
		Ambiguous genitalia	**Swelling in the groin**	**Adrenal crisis**	**Primary amenorrhea**	**No testes**	**Ambiguous genitalia history in family**	**Micropenis**	**Absence of vaginal meatus**	**Short stature**	**Total**
		n %	**n %**	**n %**	**n %**	**n %**	**n %**	**n %**	**n %**	**n %**	
46,XX DSD	21-OHD	62 70,5%		14 15,9%	2 2,3%	10 11,4%					88 100,0%
	11-OHD	4 66,7%				2 33,3%					6 100,0%
	Sertoli cell only syndrome	1 100,0%									1 100,0%
	Undetermined causes	2 100,0%									2 100,0%
46,XY DSD	SRD5A2	10 52,6%	4 21,1%		3 15,8%		2 10,5%				19 100,0%
	CAIS		5 55,6%		3 33,3%		1 11,1%				9 100,0%
	PAIS	5 83,3%			1 16,7%						6 100,0%
	STAR		1 20,0%	4 80,0%							5 100,0%
	HSD17B3	3 75,0%	1 25,0%								4 100,0%
	CYP17A1		1 100,0%								1 100,0%
	Leydig cell aplasia/hypoplasia		2 100,0%								2 100,0%
	DAX-1		2 100,0%								2 100,0%
	NR5A1 (SF-1)		2 100,0%								2 100,0%
	Progesterone treatment in pregnancy	6 85,7%	1 14,3%								7 100,0%
	Gonadal dysgenesis	4 50,0%			1 12,5%	1 12,5%	1 12,5%	1 12,5%			8 100,0%
	Mix gonadal dysgenesis	4 100,0%									4 100,0%
	Ovotestis				1 33,3%	1 33,3%			1* 33,3%		3 100,0%
	Persistent Mullerian Duct Syndrome					1 100,0%					1 100,0%
	Vanishing testis					1 100,0%					1 100,0%
	Burn	1** 100,0%									1 100,0%
	Undetermined causes	27 67,5%	4 10,0%		5 12,5%	3 7,5%		1 2,5%			40 100,0%

Sex Chromosome DSD	Mix gonadal dysgenesis	10 83,3%	1 8,3%		1 8,3%	12 100,0%
	Klinefelter	2 100,0%				2 100,0%

DSD: disorders of sex development, 21-OHD: 21-Hydroxilase Deficiency, 11-OHD: 11-beta-hydroxylase deficiency, SRD5A2: 5-alpha-reductase deficiency, CAIS: complete androgen resistance, PAIS: incomplete androgen resistance, STAR: Steroidogenic Acute Regulatory Protein, HSD17B3: 17-beta-hydroxysteroid dehydrogenase type 3 deficiency, CYP17A1: 17-alpha-hydroxylase deficiency, F: female M: male

*: Female patient with Prader stage 1 was referred for short stature, we found palpable gonads in the inguinal region and she had 46, XY chromosome structure by cytogenetic analysis

**: Patient was admitted to the council due to burn-induced ambiguous genitalia

Table 2. Etiological causes of DSD with gender assignment recommendations

		Gender Assignment			
		F n %	M n %	Follow up n %	Total n
46,XX DSD	21-OHD	80 90.9%	5 5.7%	3 3.4%	88
	11-OHD	5 83.3%		1 16.7%	6
	Sertoli cell only syndrome		1 100%		1
	Undetermined causes	2 100%			2
46,XY DSD	SRD5A2	1 5.3%	16 84.2%	2 10.5%	19
	CAIS	9 100%			9
	PAIS	2 33.3%	4 66.7%		6
	STAR	5 100%			5
	HSD17B3		3 75%	1 25%	4
	CYP17A1	1 100%			1
	Leydig cell aplasia/hypoplasia	2 100%			2
	DAX-1	2 100%			2
	NR5A1	1 50%	1 50%		2
	Progesterone treatment in pregnancy	1 14.3%	6 85.7%		7
	Gonadal dysgenesis	2 25%	4 50%	2 25%	8
	Mix gonadal dysgenesis	3 75%	1 25%		4
	Ovotestis	2 66.7%	1 33.3%		3
	Persistent Mullerian Duct Syndrome		1 100%		1
	Vanishing testis		1 100%		1
	Burn		1 100%		1
	Undetermined causes	9 22.5%	31 77.5%		40
Sex chromosome DSD	Mix gonadal dysgenesis	3 25%	8 66.7%	1 6.3%	12

	Klinefelter	1 50%	1 50%	2

DSD: disorders of sex development, 21-OHD: 21-Hydroxilase Deficiency, 11-OHD: 11-beta-hydroxylase deficiency, SRD5A2: 5-alpha-reductase deficiency, CAIS: complete androgen resistance, PAIS: incomplete androgen resistance, STAR: Steroidogenic Acute Regulatory Protein, HSD17B3: 17-beta-hydroxysteroid dehydrogenase type 3 deficiency, CYP17A1: 17-alpha-hydroxylase deficiency, F: female M: male

Table 3. Evaluation of patients' phallus length with gender assignment recommendations

	Mean Phallus Length (cm)			
Assignment	46,XX DSD	46,XY DSD	Sex chromosome DSD	Total
F	2.70 ±1.24	0.82 ±0.71	1.0 ±0.86	2.08 ±1.40
M	6.0 ±2.34	2.71 ±0.98	3.31 ±1.39	3.01 ±1.42
Follow up	4.7 ±1.7	1.80 ±0.75	2.5 ±0.70	3.0 ±1.77

DSD: disorders of sex development, F: female, M: male

Table 4. Prader classification with gender assignment recommendations

		Gender Assignment		
		F	**M**	**Follow up**
	Prader stage	n %	n %	n %
46,XX DSD	1	1 100%		
	2	7 100%		
	3	49 98%	1 2%	
	4	20 90.9%	1 4.5%	1 4.5%
	5	10 58.8%	4 23.5%	3 17.6%
46,XY DSD	1	28 90.3%	2 6.5%	1 3.2%
	2	8 44.4%	9 50%	1 5.6%
	3	2 6.1%	28 84.8%	3 9.1%
	4	2 7.4%	25 92.6%	
	5		6 100%	
Sex Chromosome DSD	1	2 100%		
	3	1 14.3%	4 57.1%	2 28.6%
	4		5 100%	

DSD: Disorders of sex development, F: female, M: male

Figure 1. Gender orientations and gender assignment recommendations

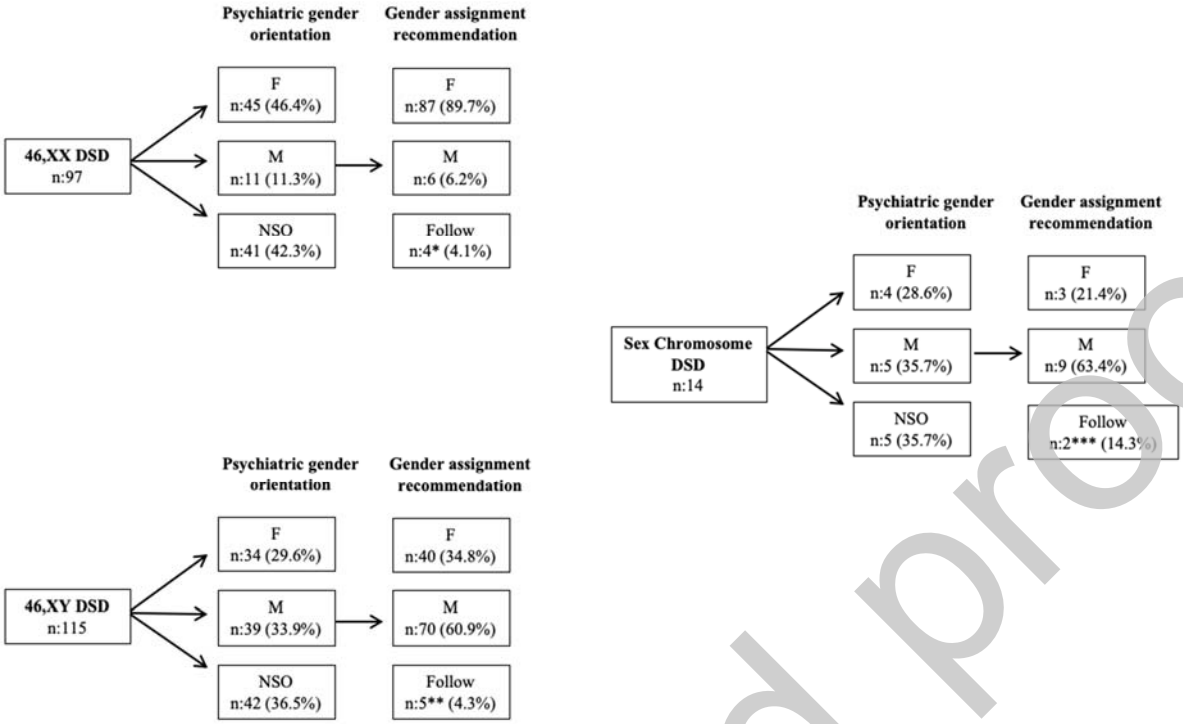

Figure 1. Gender orientations and gender assignment recommendations (DSD: disorders of sex development, F: female, M: male, NSO: no sexual orientation)
*: Two of the 3 cases with 46, XX related to 21-OH deficiency were raised as a male and their families insisted on an assignment recommendation as the male gender. The other one case had female gender orientation, but the family wanted to raise as the male gender. The remaining one 46,XX DSD patient had 11-OH deficiency, and raised as the male gender. Moreover, patient's family wanted to raise as the male gender although the patient had menstrual bleeding.
**: For 2 cases with 46,XY DSD diagnosed with 5-alpha reductase deficiency a follow-up recommendation was made, who were raised as female gender instead of male gender by their parents. Families were persistently wanting for a female assignment to be made. The other two 46,XY DSD cases had a diagnosis of gonadal dysgenesis and had not yet developed a gender orientation. The one 46,XY DSD patient had 17-beta-hydroxysteroid dehydrogenase type 3 deficiency, was raised as a female and the family asked for as the male gender assignment.
***: The one Klinefelter syndrome case was raised as a female and her family wanted to rise as the female gender. The other one patient was mixed gonadal dysgenesis and had no gender orientation yet.