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Research Article

Pediatric Transgender Care: Experience of a Swiss Tertiary Center Over the Past Decade

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Abstract

Youth with gender dysphoria are increasing in numbers worldwide. We investigated the cohort of gender dysphoric youth for this trend referred to a Swiss University Children's Hospital and assessed clinical characteristics and outcome of hormonal treatments at the Division of Pediatric Endocrinology. The retrospective study included 57 pediatric individuals referred between 2012 and 2021. Characteristics of 28 hormonally treated subjects with a diagnosis of transsexualism (ICD-10) were assessed. The number of subjects with gender dysphoria and with a diagnosis of transsexualism increased over the years, but the increase was less pronounced in the latter. A similar trend was found in a nationwide survey for the nine largest pediatric endocrine units in Switzerland. Of the 28 hormonally treated subjects in our center, 78% were trans males and 61% had psychiatric comorbidities. Height and BMI of individuals with transsexualism were normal and did not change under hormonal therapies in the first years. Thus, our study confirms the world-wide trend of increasing numbers of adolescents with gender dysphoria and transsexualism in Switzerland, and the predominance of trans males over trans females. In our cohort, however, numbers of subjects receiving hormonal treatments did not rise proportionally, possibly due to strict diagnosis and psychological assessments before referral. Similar to other studies, we also found an alerting high prevalence of psychiatric comorbidities that needed additional treatment. Therefore, hormonal treatments should only be offered to trans gender youth after careful evaluation by specialized mental health care professionals as recommended in current guidelines.

Keywords: Gender Dysphoria; Gender Incongruence; Pediatric Transgender; Pediatric Endocrinology; GnRH analogue; Gender-Affirming Hormones.

Introduction

The number of youths with gender dysphoria (GD) and gender identity disorders seeking hormonal or other care seems to be rising in many countries worldwide [1-5].Therefore, efforts are directed towards setting standards of care and identifying areas of uncertainties in order to provide safe treatments in the short and long-term, and to promote corresponding research. Terminology in the field is a sensitive issue, varies and has been updated recently by the World Health Organization (WHO) [6]. In the 10th edition of the International Classification of Diseases (ICD-10) of the WHO [7], which was in use until 2021, the diagnostic category was transsexualism. Therein transsexualism has been defined as the "desire to live and be accepted as a member of the opposite sex, usually accompanied by a sense of discomfort with, or inappropriateness of, one's anatomic sex, and a wish to have surgery and hormonal treatment to make one's body as congruent as possible with one's preferred sex". In the current version of ICD-11 [6], which is in effect since 2022, the diagnostic category "transsexualism" has been replaced with "gender incongruence" (GI), with the more comprehensive definition of "marked and persistent incongruence between an individual's experienced gender and the assigned sex".

The typically binary sex (female or male) is usually recorded at birth based on the appearance of the external genital organs. By contrast, gender identity refers to the personal sense of self in a holistic sense of the whole spectrum of male, female, in-between or beyond, and it can be binary or non-binary [8]. The development and self-recognition of gender identity is part of the individual psychological and sexual development, for which awareness mostly arises with puberty, although earlier or later occurrence is also possible [9-11]. To diagnose transsexualism, an assessment by a mental health professional has been recommended, especially in youths [12]. If desired, the individual may then be referred to an endocrinologist for hormonal therapies. Although the etiology of GD/GI and transsexualism has been investigated by several studies [13-21], it remains unsolved. Likewise, the exact prevalence of GD and transsexualism is unclear.

In the adult population, the prevalence of treated individuals with GD is 4.6 in 100,000 and shows a preponderance of trans females over trans males of 6.8 to 2.6 per 100,000, respectively [22]. In youth, the estimated prevalence is based on self-reported surveys and ranges from 0.5% to 2.7% [1, 23-25], with an overall increase in the last two decades [1, 2, 26]. More specifically, the self-reported prevalence for transsexualism has been reported with 1.2% to 1.3% [23, 24], and for GD with 2.7% [27]. Adolescents with GD and transsexualism have a statistically significant higher prevalence of psychiatric disorders and suicidal attempts compared to their cisgender peers [28-32]. A positive effect of gender-affirming hormones (GAH) has been suggested in the adult population [33]. Likewise, improved psychosocial functioning and decreased depression and anxiety were recently reported after 2 years of GAH treatment in GD youths [34].

The first report on hormonal and surgical treatment of transgender adults dates back to the early 1900s. However, only in 1979 the now-called World Professional Association for Transgender Health (WPATH) published the first standards of care. This guideline for professionals has since been updated to the 8th Version in 2022 [35]. In the pediatric and adolescent transgender population, the first report on hormonal interventions came from The Netherlands in 1987 [36]. It describes a two-step approach for hormonal treatments. This approach is still recommended in current guidelines from the Endocrine Society [12], with step 1 comprising of pubertal suppression with a gonadotropin-releasing hormone analogue (GnRHa), and step 2 that of GAH therapy (testosterone or estrogen). In addition, step 3 consists of surgical treatments, which should only be offered to adults.

Hormonal treatments of youth with transsexualism may not only have positive effects. Possible adverse effects on the developing brain and on psychological and psychosocial formation are critically discussed [37-40]. Other adverse effects may concern growth, body composition and physiognomy, fertility, bone health, cardiovascular as well as cancer risk [41-47]. Data on most of these topics are scarce and controversial; thus, further studies are needed.

This study aimed at characterizing individuals referred to a pediatric tertiary care center in Switzerland for GD during the last decade and comparing the findings of youth diagnosed and treated for transsexualism to other cohorts published in the literature.

Materials and methods

This observational study was conducted in a tertiary care center at the University Children's Hospital Bern, Switzerland, which started offering interdisciplinary transgender care in 2012. This center is one of the five University Hospitals in the country providing tertiary care to about 1.5 million of the Swiss population. Retrospective data analysis was allowed without informed consent under ethical approval BASEC ID 2016-01210. Inclusion criteria were age <18 years and referral to our center for GD. Exclusion criteria for being part of the group of hormonally treated individuals were chromosomal or anatomical anomalies (difference of sex development, DSD), not hormonally treated, or not treated at our center.

Referred children and adolescents were first evaluated by a mental health professional, who assessed GD and specifically diagnosed transsexualism according to the ICD-10 [7]. Only individuals with a diagnosis of transsexualism desiring a hormonal therapy were then seen in our endocrine clinic. Clinical assessment included medical history, physical exam, and laboratory analyses as recommended [12]. Only hormonal therapies of step 1 and 2 were offered, while surgical interventions (step 3) were not supported by our team. Clinical and anthropometrical data of children and adolescents were extracted from the electronic health record system from January 2012 to September 2021. In general, data are shown as absolute numbers, median, and range. Standard deviations (SD) of height and body mass index (BMI) were calculated for the sex recorded at birth according to the charts of the WHO [48]. The pubertal development was assessed by the Tanner stage [49, 50]. Bone mineral density (BMD) was evaluated with bone densitometry (DXA) of hip and spine according to the sex recorded at birth and expressed conforming to NHANES (National Health and Nutrition Examination Survey) and WHO charts [48, 51]. The results of DXA were categorized as “low” or “normal” BMD according to the International Society of Clinical Densitometry [52] with low BMD describing at least one of the two z-scores ≤ -2.0 SD.

In addition, a short questionnaire was sent to the leaders of the pediatric endocrine units of the nine largest children’s hospitals in Switzerland, asking for minimal information on their GD and transgender cohorts (e.g., size of cohort, numbers of new referrals per year in the past 5 to 10 years) to compare our data at a national level.

Data analysis was mostly descriptive taking the small numbers into account. Nevertheless, significance of increase in the number of GD and transsexual youths over the years was calculated with a linear regression. A paired t-test was used to analyze for statistically significant differences of height and BMI (on normalized data in SD) between step 1 and 2 of therapies in the GAH-treated subgroup. Statistical significance was set at $p \leq 0.05$. Statistical analysis was performed with the Python package stats model [53].

Results

From 2012 to 2021, 57 children and adolescents were referred to the University Children Hospital for GD. Of these, 41 were biologic females, 14 biologic males, and two individuals had a diagnosis of a 46, XY DSD, recorded female at birth. The median age at referral was 14.9 years (range, 4.6-17.9 years). Of the 57 individuals evaluated by our mental health professionals, 45 had a diagnosis of transsexualism in conformity with ICD-10 [7] and 31 received hormonal treatments (Figure 1), 28 at our endocrine center (Table 1). Over the past 10 years, numbers of subjects with GD and transsexualism increased statistically significant at our center, while numbers of hormonally treated subjects with transsexualism increased less pronounced (Figure 2). Further characteristics of the GD group and the subgroup of hormonally treated individuals with transsexualism are depicted in Figure 3. Age and Tanner stage at referral and at the start of hormonal therapy as well as frequency of psychiatric comorbidities are shown. Referral for GD occurred mostly after 10 years of age and after puberty onset; only 7 children (out of them 4 with transsexualism) were seen at a younger age (Fig. 3A, B). Pubertal hormone suppression was started at the earliest at 10 years of age and a Tanner stage 2, but in most patients after 14 years of age and a Tanner stage 4 (Fig. 3D, E). Cross-sex GAH treatment was started at the earliest at 14 years of age (Fig. 3D). Psychiatric comorbidities were diagnosed in 42% of subjects in the GD group and in 61% in the subgroup of hormonally treated youths with transsexualism (Fig. 3C, F). Additional data for analysis were only available from the group of youths with transsexualism receiving hormonal treatment at our center (Table 1). Of these 28 teenagers, 22 (78%) were trans males and 6 (21%) trans females, 17 (61%) had psychiatric comorbidities, and drug abuse was recorded in three individuals. Psychiatric comorbidities were assessed by certified psychiatrists and specialized psychologists before being referred to the endocrine clinic and included mainly depression/self-harm attitude (n = 13), autism spectrum- and attention-deficit/hyperactivity disorders (n = 4). In the cohort, there were suicidal ideations (n = 3), but no suicidal attempts were recorded.

ID	Sex recorded at birth	Identity	Age 1st contact	Step 1							Step 2						Psychiatric comorbidities
				Age year	Tanner	Height cm	Height SDS	Weight kg	BMI kg/m²	BMI SDS	Age year	Height cm	Height SDS	Weight kg	BMI kg/m²	BMI SDS	
1	Female	Transmale	15.7	15.7	5	160.4	-0.29	49.4	19.2	-0.52	17.43	161.1	-0.28	44.1	16.99	-1.93	D
2	Male	Transfemale	12.9	11.8*	2	145.5	-1.26	33.9	16.01	-1.2	14.31	150.5	-1.78	37.7	16.64	-0.87	no
3	Male	Transfemale	14.2	14.3	4	170.5	0.62	48.5	16.7	-1.24	14.96	171.5	0.22	53	18	-0.79	no
4	Female	Transmale	12.8	12.9	5	161.5	0.95	62.9	24.1	1.48	n/a						no
5	Female	Transmale	15.2	15.2	5	171.8	1.5	49.6	16.8	-1.59	17.08	173	1.56	54.4	18.2	-1.21	D, M
6	Male	Transfemale	15.6	15.6	4	169.6	-0.22	85.4	29.7	2.17	n/a						no
7	Female	Transmale	16.8	16.8	5	168.1	0.81	95.2	33.7	2.81	n/a						D
8	Female	Transmale	14.8	15.0	5	167	0.88	54.4	19.5	-0.23	n/a						no
9	Female	Transmale	14.1	14.1	5	162.5	0.38	48	18.2	-0.6	n/a						D
10	Female	Transmale	10.0	10.4	2	143	0.44	40.5	19.8	0.92	14.04	160.4	-0.01	59	22.9	0.95	no
11	Female	Transmale	14.6	14.7	5	169.5	1.23	57.5	20	0.1	16.1	169.7	1.1	63.6	22.1	0.48	D
12	Male	Transfemale	14.5	14.5	4	166	0	53.95	19.6	0.02	n/a						no
13	Female	Transmale	15.7	15.7	5	-		55	-	-	16.4	169.7	1.07	60.45	21	0.11	Asperger
14	Female	Transmale	15.0	15.0	5	154.2	-1.14	43.3	18.2	-0.65	16.1	155.5	-1.09	55.6	23	0.69	D
15	Female	Transmale	13.5	13.6	5	161.7	0.53	54.75	20.9	0.59	16.1	168.4	0.9	59.45	21	0.08	no
16	Female	Transmale	14.9	15.1	4	161.9	0.07	45.8	17.5	-1.1	n/a						D
17	Male	Transfemale	16.0	15.5*	5	186.6	1.94	55.2	15.9	-2.41	16.47	187.4	1.98	57	16.2	-2.26	Asperger
18	Female	Transmale	10.3	10.3	3	153	1.82	39	16.7	-0.05	14.08	167	1.12	53.7	19.3	-0.12	ADHD
19	Female	Transmale	15.0	15.0	5	161.2	-0.1	57	21.9	0.57	16.52	161.7	-0.16	56.9	21.8	0.34	D
20	Female	Transmale	14.9	14.2*	5	160.7	-0.19	97.4	37.7	3.19	n/a						D
21	Female	Transmale	13.2	13.4	5	157.1	-0.15	73.5	29.8	2	15.59	159	-0.51	74.85	29.6	1.76	D
22	Male	Transfemale	15.5	15.7	4	181.5	1.09	48.3	14.6	-3.67	16.58	181.5	0.94	51	15.5	-3.08	Asperger
23	Female	Transmale	13.8	13.9	4	144	-2.42	35.9	17.3	-0.78	16.68	151	-1.83	46.6	20.4	-0.14	D, M
24	Female	Transmale	15.2	16.0	5	161.2	-0.2	67.55	26	1.45	17.55	161	-0.3	71.9	27.7	1.87	no
25	Female	Transmale	17.2	17.2	5	180.5	2.7	71.4	21.9	0.27	n/a						no
26	Female	Transmale	14.9	15.1	5	160.4	-0.17	48.3	18.8	-0.53	15.84	161.3	-0.15	46.7	17.9	-1.04	no
27	Female	Transmale	15.5	15.6	5	167.9	0.88	85.45	30.3	2.28	17.4			97.1			D
28	Female	Transmale	16.2	16.4	5	169.6	1.06	62.55	21.7	0.29	n/a						D

Transfemale (n = 6)	Median	15.0	15.0	4	170.0	0.3	51.2	16.3	-1.2	15.7	176.5	0.58	52.0	16.4	-1.56
	Range	(12.9;16.0)	(11.8;15.7)	(2;5)	(145.5;186.6)	(-1.26;1.94)	(33.9;85.4)	(14.6;29.7)	(-3.67;2.17)	(14.3;16.6)	(150.5;187.4)	(-1.78;1.98)	(37.7;57)	(15.5;18)	(-3.08;-0.79)
Transmale (n = 22)	Median	14.9	15.0	5	161.5	0.4	54.9	20.0	0.27	16.2	161.3	-0.15	57.9	21.0	0.11
	Range	(10.0;17.2)	(10.3;17.2)	(2;5)	(143;180.5)	(-2.42;2.7)	(35.9;97.4)	(16.7;37.7)	(-1.59;3.19)	(14.0;17.5)	(151;173)	(-1.83;1-56)	(44.1;97.1)	(17;29.6)	(-1.93;1.87)

Table 1: Characteristics of subjects with transsexualism hormonally treated at our center (n = 28); Psychiatric comorbidities: 3 main categories: D: Depression/Suicidal/Self-harm; ADHD (attention-deficit/hyperactivity disorders)/Asperger; M: mental disorders (ID 5 dissociative disorders, ID 23 unclear diagnosis). SDS: standard deviations, calculated based on sex recorded at birth. n/a: not applicable

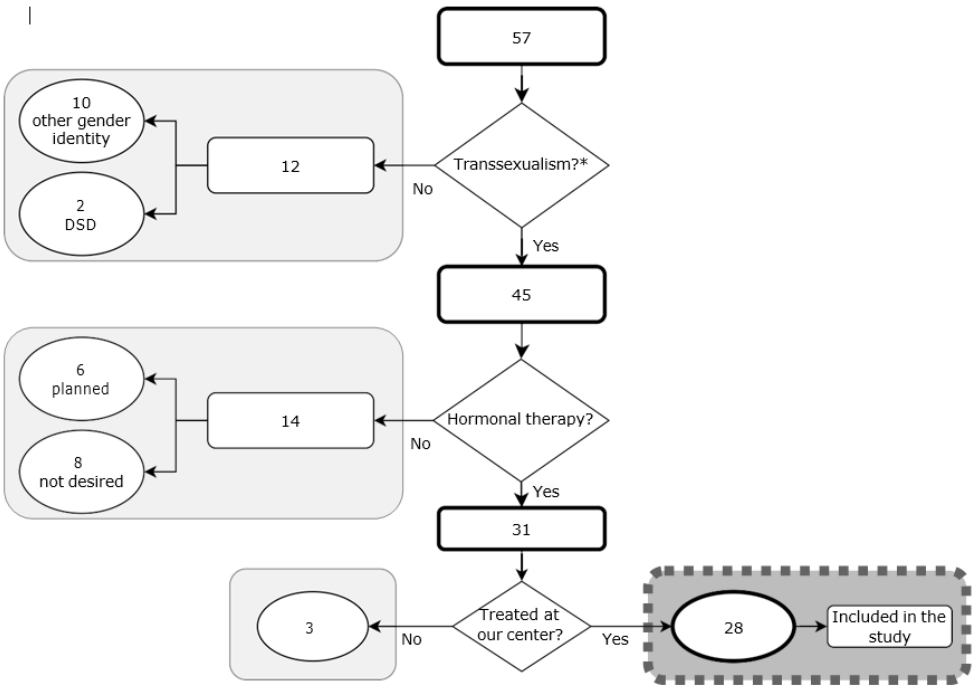

Figure 1: Selection of individuals included in the study. 57 individuals were referred to our center for gender dysphoria (GD), 45 were diagnosed with transsexualism (ICD-10), and 31 received hormonal treatment, 28 at our center. Subjects with a diagnosis of DSD (Differences of sex development) were excluded; *ICD-10 [7]

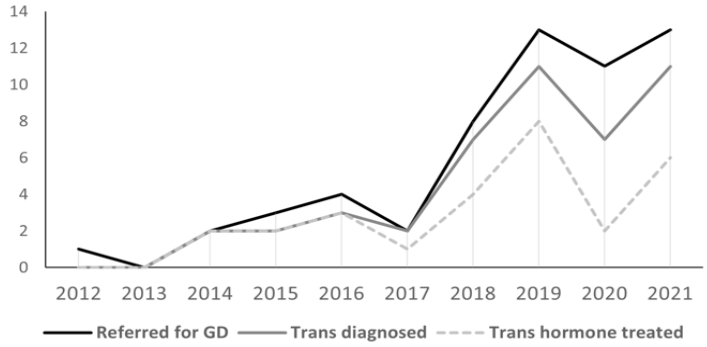

Figure 2: Annual numbers of referrals. Numbers for gender dysphoria (GD), diagnosed subjects with transsexualism (ICD-10), and hormonally treated subjects are shown.

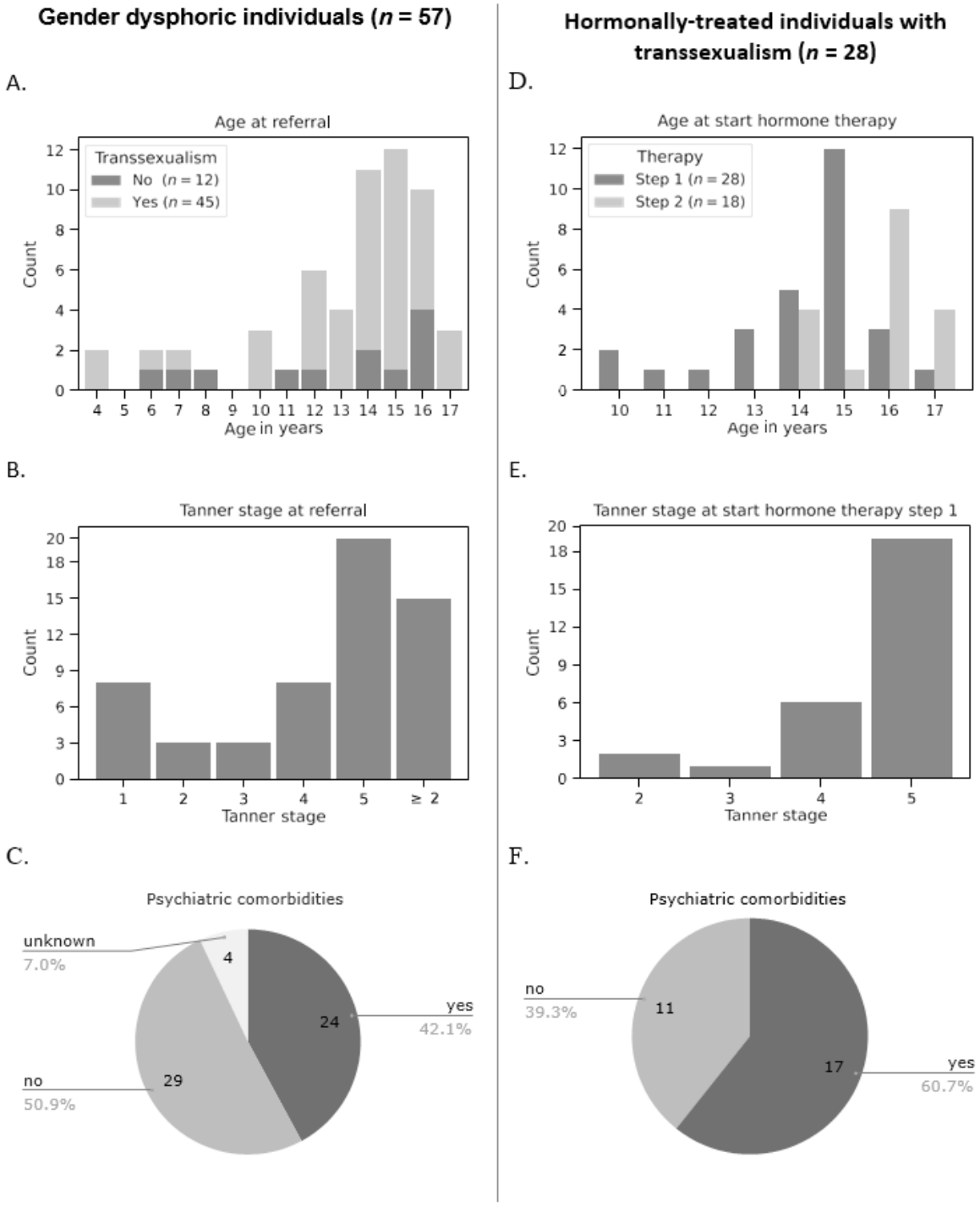

Figure 3: Characteristics of the study cohort given for all individuals referred for gender dysphoria (A-C, left panel, n = 57) and for hormonally treated transsexual youth (D-F, right panel, n = 28). A. Age at referral. B. Tanner stage at referral. C. Psychiatric comorbidities. D. Age at start hormonal therapies (step 1 and step 2); E. Tanner stage at start GnRHa, and F. Psychiatric comorbidities in transsexual subjects.

The median age at start of pubertal suppression therapy (step 1) was 15.0 years (range,10.3-17.2y) and the respective Tanner stage was on average 4 (range, 2-5) (Table 1 and Figure 3D, E). Two individuals experienced minor side effects with the first step of therapy, one with local aseptic abscesses at the injection sites of the GnRHa, and one with a transient rise in serum transaminase levels. There were no major side effects reported. Eighteen individuals received GAH therapy step 2 at a median age of 16.4 years (range, 14-17.6y) (Table 1, Figure 3D). The average interval between start GnRHa suppression therapy (step 1) and GAH therapy (step 2) was 18 months (range, 6-45 months).

In our small cohort, height, weight, and BMI were within normal ranges of the corresponding sex recorded at birth in both trans females and trans males, and did not change statistically significant from step 1 to 2 of hormonal therapies, with the exception of a reduction of the BMI in trans females ($n = 4$, $p = 0.03$) (Table 1). Fertility preservation in theory was offered to all individuals, but specific information on this topic was mostly missing in the patient charts of our teenagers. Thus specific data were only available in ten individuals; six were seen by the fertility specialists, of which three (two trans males and one trans female) then underwent fertility preservation procedures, while three (trans males) abstained.

Data on bone densitometry were available in 15 individuals (12/22 trans males, 3/6 trans females; overall 54%). Ten had a normal result and five showed a low BMD (z-score ≤ - 2.0 SD) according to z-score charts of their sex recorded at birth [51]. Of the five individuals with low BMD, two received GAH therapy step 2 (one trans male and one trans female), while three were only treated with a GnRHa (step 1) at the time of assessment (one trans male and two trans females). No pathological fractures were reported. Two of the 28 hormonally treated teenagers (one trans male and one trans female; 7%) decided to stop the GnRHa suppression therapy after a few months. Both of them still live in their sex recorded at birth at this time point.

Four individuals opted for an additional surgical therapy (step 3). Three of them immediately after transitioning to adult care at the age of 16.5, 18, and 18.5 years (2 mastectomies, and 1 breast augmentation and genital reconstruction surgery, respectively). The fourth individual opted for a surgical operation (mastectomy) at the age of 15 years.

To put our data in a broader, nationwide perspective, we performed a survey with a simple questionnaire, which was addressed to the heads of pediatric endocrine units at the nine largest children's hospitals in Switzerland. The 9 centers reported that they started offering endocrine care and hormonal treatments to children and youths with transsexualism between 2016 and 2022. At the end of 2022, they estimated to provide hormonal treatments to about 1-130 subjects (median 25 per center). Centers that offered care for more than 5 years reported increasing numbers of new referrals.

Discussion

This is the first study showing that the number of youths seeking care for transsexualism is increasing in Switzerland as in many other countries. Currently, however, the number of subjects receiving hormonal treatments did not rise proportionally. Similar to others, we have also noticed a higher rate of trans males than trans females, and more psychopathologies in these youths. It has been suggested that the overall increase in numbers of pediatric individuals with transsexualism may be explained by a net increase of numbers of trans males [54, 55]. Moreover, a recent study from the UK found that the sex ratio of trans females to trans males differed with the age at referral, with a higher rate of trans females in children <12 years of age compared to adolescents [56].

The high prevalence of psychiatric comorbidities in GD youth has raised suspicion that the symptom of GD might be abused to express other psychological discomfort [57], but this has been strongly debated. Other explanations for the increase include the wider awareness and the establishment of specific school programs enhancing social acceptance of the topic. In our study cohort, we found a high number of psychiatric comorbidities, e.g., 61% in hormonally treated youth, similar to other small cohort studies [55, 58]. This number compares to 50% in transsex adults in a larger cohort [59] and to 30% in a pediatric cohort [60].

Adolescence is a critical and limited period for attaining final height, body shape and composition, as well as bone mineral density (BMD), which may be irreversibly changed by GnRHa and cross-sex hormone therapies depending on the age and pubertal stage when they are started. Data on these topics are scarce. In our cohort, we observed no effects on growth and BMI, but in some subjects on GnRHa treatment, a low BMD was found. Diminished growth velocity with a slightly decrease in final height for both natal sexes have been reported [46, 61].

Likewise, a negative impact on BMI has been suggested [62]. A decrease of the lumbar spine BMD z-score in the first two years of GnRHa treatment with an incomplete catch-up after starting of GAH therapy has been described [41, 63], while a better catch-up was seen in a more recent study after a longer follow-up [47].

Another great concern about GAH therapy is the risk of a future regret. This risk is difficult to assess and varies broadly in different studies depending on the definition used as well as with the length of follow-up. Some cohort studies (adult and pediatric) found a low rate of 0.01 to 0.5% [26, 64], while more recent studies in the adult population reported a high risk rate of 6.9 to 29.8%, when taking into account the percentage of subjects who discontinued GAH therapy [65, 66]. Underreporting of the risk seems likely, as a recent study showed that the majority of individuals who

detransitioned (76%) did not inform their clinicians [67]. In our cohort, we had 2 subjects who stopped GnRHa therapy after a few months, but did not regret the treatment as it allowed them more time to think and decide on their gender identity.

Still, there are several ethical issues with respect to the irreversible physical effects and effects on future fertility of GAH therapies, especially when offered to youth, in whom the sexual and neuropsychological development is not completed. It is discussed whether adolescents' capabilities of decision making are sufficiently mature for making critical and irreversible treatment choices. In fact, important neuropsychological and gender-forming developments occur during adolescence [55, 68-70] and the impact of hormonal treatments on these processes is largely unknown. An effect on cognitive function and spatial reference memory was shown in animal models [37]. In humans, GAH treatment had no effect on cognitive function, but prompted a sex-atypical brain activation during executive function [38]. In trans males, a statistically significant increase in visuospatial ability was reported [39].

Our study suffers from small numbers and the retrospective design. On the other hand, the single-center setting bears the advantage that the initial evaluation of all study subjects was performed by only two mental health care professionals in a very consistent fashion. Similarly, the hormonal treatment was provided by a small team of pediatric endocrinologists.

Conclusion

We add Switzerland to the numerous countries, in which numbers of youth with transsexualism increased statistically significant in the past decade. The Swiss cohort is characterized by a high rate of transmales and a worrisome high rate of additional mental health problems. In our experience, not all youth with a confirmed diagnosis of transsexualism desire hormonal treatments.

Acknowledgment

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Disclosure

Ethics Guidelines

Ethical approval was under BASEC ID 2016-01210.

Conflict of Interest

The authors declare no conflict of interest.

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Consent to participate

Informed consent was not required for this study on minimal, anonymized data collected for institutional audit.

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