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Research

Quality of Life and Psychological Well-Being in Child and Adolescent with Disorders of Sex Development

Şentürk Pilan B et al. Quality of Life & Disorders of Sex Development

Birsen Şentürk Pilan[1], Burcu Özbaran[1], Didem Çelik[1], Tuğçe Özcan[1], Samim Özen[2], Damla Gökşen[2], İbrahim Ulman[3], Ali Avanoğlu[3], Sibel Tiryaki[3] , Hüseyin Onay[4] , Özgür Çoğulu[4] , Ferda Özkınay[4] , Şükran Darcan[2]
[1]Birsen Şentürk Pilan, Burcu Özbaran, Didem Çelik and Tuğçe Özcan: Department of Child and Adolescent Psychiatry, Ege University Faculty of Medicine, İzmir, Turkey
[2]Samim Özen, Damla Gökşen and Şükran Darcan: Department of Pediatric Endocrinology, Ege University Faculty of Medicine, İzmir, Turkey
[3]İbrahim Ulman, Ali Avanoğlu and Sibel Tiryaki: Department of Pediatric Surgery, Ege University Faculty of Medicine, İzmir, Turkey
[4]Hüseyin Onay, Özgür Çoğulu and Ferda Özkınay: Department of Medical Genetics, Ege University Faculty of Medicine, İzmir, Turkey

What is already known on this topic?
Articles about of life in DSD patients who were evaluated with qualitative and quantitative tools in developing and developed countries were reviewed and a broad spectrum of QoL emerged among lower, better or similar QoL results than the normal population. No study in our country evaluating the QoL of children and adolescents with DSD has been found.

What this study adds?
In our study, there was no significant difference between 46 XX DSD and 46 XY DSD groups both child and parent Total PedsQL scores. In the subscale scores, the PedsQL Physical Functionality Score filled by children was significantly lower in the 46 XX DSD group than in the 46 XY DSD group (p=0.01).
PedsQL School Functionality Score, which is filled by children and adolescents, is significantly lower in the group with a psychiatric diagnosis compared to the group without a psychiatric diagnosis. In addition, PedsQL Total Score, PedsQL Emotional Functionality Score, PedsQL Social Functionality Score, PedsQL School Functionality Score filled by parents in the group with psychiatric diagnosis are significantly lower than the group without psychiatric diagnosis.
Considering our results, it is seen that psychiatric disorders in patients with DSD are the most important factor affecting the quality of life.

ABSTRACT
Objective: The aim of this study was to assess the quality of life and psychological well-being in child and adolescent with disorders of sex development (DSD).
Methods: Sixty two cases aged 2-18 years who were followed by multidisciplinary DSD team were included. All participants and their parents were requested the complete Pediatric Quality Of Life Inventory (PedsQL) and the Strengths and Difficulties Questionnaire. The psychiatric diagnoses of the patients were evaluated according to Schedule for Affective Disorders and Schizophrenia for School-Age Children/Present and Lifetime Turkish Version.
Results: There was no significant difference between 46 XX DSD and 46 XY DSD groups both child and parent Total PedsQL scores. In the subscale scores, the PedsQL Physical Functionality Score filled by children was significantly lower in the 46 XX DSD group than in the 46 XY DSD group (p=0.01). There was a psychiatric diagnosis in 25.8% cases. The PedsQL School Functionality Score filled by children in the group with psychiatric diagnosis was significantly lower than the group without psychiatric diagnosis (p = 0.018). In the group with psychiatric diagnosis, the PedsQL Total Score and the subscale scores (Emotional Functionality Score, Social Functionality Score, School Functionality) filled by parent were significantly lower than the group without psychiatric diagnosis.
Conclusion: Our study is important to emphasize that psychiatric disorders in DSD patients negatively affect the quality of life. Psychiatric support and counseling of multidisciplinary team are very important in DSD cases.
Key Words: Disorder of sex development, quality of life, psychiatric disorder, child and adolescent

Birsen Şentürk Pilan, Department of Child and Adolescent Psychiatry, Ege University Faculty of Medicine, İzmir, Turkey, Ege Üniversitesi Tıp Fakültesi Hastanesi Çocuk ve Ergen Ruh Sağlığı ve Hastalıkları Anabilim Dalı, Bornova, İzmir, 35100
05055250939/ 0232 399 13 66
drbirsensenturk@yahoo.com
0000-0002-4580-7655
29.06.2020
06.09.2020

INTRODUCTION
Rare congenital conditions that are noticed by incompatibility of chromosomal, gonadal, and phenotypic gender characteristics are classified as disorders of sex development (DSD) (1). The incidence of disorders of sex development is approximately 1 in 4500-5500 (2). Studies to date have focused on psychosexual outcomes such as gender dysphoria, sexual

function status and satisfaction of surgical outcomes in individuals with DSD; very few really assessed general well-being or social participation (3). Long-term psychological, physical and social consequences of young people with DSD are uncertain (4).

Health-related quality of life (HRQOL) has a multidimensional structure that includes various core states (eg physical functionality and symptoms, psychological and emotional state and social functionality) that reflect subjective assessments of the patient and his/her family (5). HRQOL measures are increasingly used to determine the impact of medical interventions on compliance and psychosocial well-being (6,7). An important point to guide the sex assignment in newborns with indeterminate genital organs is the quality of life (QoL) of these patients in adulthood. Rare occurrence of most DSD conditions complicates long-term follow-up of affected patients during adulthood. In the study of Amaral et al**.(8),** articles about ~~of~~ life in DSD patients who were evaluated with qualitative and quantitative tools in developing and developed countries were reviewed and a broad spectrum of QoL emerged among lower, better or similar QoL results than the normal population.

In addition most of the patients dissatisfaction is not associated with poor management of the disease or with the assigned gender. A better understanding of their condition, cooperation with the family and medical team lead to increased satisfaction with treatment. The review of Amaral et al. shows that a talented multidisciplinary team is necessary to deal with these patients throughout their diagnosis and life, and cooperation with patients and parents is crucial (8).

No study in our country evaluating the QoL of children and adolescents with DSD has been found. In our study, it was aimed to evaluate the health-related quality of life in children and adolescents in this disease group and to shed light on future health interventions and approaches.

METHODS

In this one year study; 62 cases aged 2-18 years who were followed by multidisciplinary DSD team and were refered to Ege University Department of Child and Adolescent Mental Health and Diseases were included. All participants and their parents were requested the complete Pediatric Quality Of Life Inventory (PedsQL). The Strengths and Difficulties Questionnaire (SDQ) related to emotional and behavioral problems were filled **by** the parents and teachers of 4-17 years old cases and it was filled by the cases above 11 years old. The psychiatric diagnoses of the patients were evaluated according to Schedule for Affective Disorders and Schizophrenia for School-Age Children/Present and Lifetime Turkish Version (K-SADS-PL-T) and Diagnostic and Statistical Manual of Mental Disorders 5 (DSM 5) diagnostic criteria.

The classification of the medical diagnosis of patients with DSD was made according to the Lawson Wilkins Pediatric Endocrine Society and the European Society for Pediatric Endocrinology Consensus Statement (9).

In order to make statistical comparisons between groups, endocrine diagnoses were gruped into four groups: 46 XX DSD Group, 46 XY DSD Group, Syndromic Group and Chromosomal Disorder Group. However, since there were not enough cases in the Syndromic and Chromosomal Disorder groups they were removed during the statistical evaluation and the comparisons between the scales were made between the 46 XY DSD and 46 XX DSD groups.

Sociodemographic datas including age, gender, school, mother, father, etc. were recorded in the case data form prepared by the authors. Following a full description of the study and study procedure, patients who could give informed consent and all parents were asked to provide written consent. The study was approved by Ege University Medical Research Ethics Committee (19-10.1T/56, 16.10.2019).

TOOLS

Schedule for Affective Disorders and Schizophrenia for School-Age Children/Present and Lifetime Turkish Verison (K-SADS-PL-T):

A semi-structured interview form, K-SADS-PL-T was developed by Kaufman et al. (1997) [10] in order to determine the past and present psychopathologies of children and adolescents according to DSM-IV [11] diagnostic criteria and validity and reliability study for Turkish sample was conducted by Gökler et al. (2004) [12]. In K-SADS-PL-T, the presence and severity of symptoms are decided by combining the views of the child / adolescent, parents and clinician. During the study period two clinicians confirmed the psychiatric diagnoses according to DSM 5 diagnostic criteria (13).

Pediatric Quality-of-Life Inventory (PedsQL): HRQOL was assessed using the PedsQL which contains 23 items in four subscales including physical (eight items), emotional (five items), social (five items) and school (five items) functions. There are four different forms of the scale for the 2–4, 5–7, 8–12 and 13–18 age groups. Children rated how often the item has been a problem for them in the past 1 month using a five-point response-scale format (0 = never a problem, 1 = almost never a problem, 2 = sometimes a problem, 3 = often a problem, 4 = almost always a problem). The scores **ranged** from 0 to 100, with higher scores indicating better HRQOL. The total PedsQL score was computed as the sum of all items divided by the number of items answered. **Internal consistency (Cronbach alfa=0.70-0.89) and clinical reliability are high.** (14). The reliability and validity of the Turkish version of PedsQL in adolescents (for the 8–12 and 13–18 age groups) were studied by Memik et al. (15, 16) **while 2-7 years version was studied by Üneri ÖŞ. (17)**

Strength and Difficulties Questionnare (SDQ): This scale is a scale used in screening emotional and behavioral problems in children. It was developed by Goodman in 1997 (~~17~~) **(18)** and it contains 25 questions. These questions are under five subtitles, each five questions; Emotional Problems, Attention Deficit and Hyperactivity, Behavioral Problems, Peer Problems and Social Behaviors. This questionnaire has parent and teacher form **for** ages 4-17 and the adolescent's self-filled forms for the ages 11-17. The Turkish validity and reliability study of this questionnaire parent and adolescent forms was conducted **(19, 20).** However, the Turkish validity and reliability of the teacher form was not done to the best of our knowledge.

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS 22 package program. The statistical significance was performed using T Test for numerical variables, Man Whitney U test for non-normal distributions, cross table, Pearson chi-square test and Fisher's exact test for categorical variables. The normality assumption of quantitative data was separately controlled in the groups by Shapiro-Wilk test. $P<0.05$ values will be considered statistically significant. Variable correlation was evaluated by Pearson Correlation if normal distribution was detected, and Spearman correlation if it is not achieved.

RESULTS

The average age of 62 cases participating in the study was 9.70±4.18 **years.** Thirty six (58.1%) of the cases were raised in female sex and 26 (41.9%) in male sex. Sociodemographic characteristics are summarized in Table 1.
Endocrine diagnoses of the cases were 46 XX DSD in 30.6% (n = 19), 46 XY DSD in 67.7% (n = 42) and chromosome disorders in 1.6% (n = 1). Endocrine diagnoses are summarized in Table 2.
There was a psychiatric diagnosis in 16 (25.8%) cases, and there was no psychiatric diagnosis in 46 (74.2%) cases. **The average age of our patients with a psychiatric diagnosis was 11 (± 4.02) years, and the average age of our patients without psychiatric diagnosis was 9.26 (± 4.17) years.**
The most common psychiatric diagnosis was attention deficit and hyperactivity disorder (ADHD) (n = 13, 21.0%). Depressive disorder (n = 2, 3.2%), mental retardation (n = 2, 3.2%), anxiety disorder (n = 3, 4.8%), autism (n = 1, 1.6%), specific learning disability (n = 1, 1.6%) were the other psychiatric diagnoses.
PedsQL and SDQ Scores:
Scales comparisons were made between 46 XY DSD (n=38, 66.7%) and 46 XX DSD groups.
In the 46 XX DSD group; CAH (n=15, 24.2 %), virilizing tumor lutheoma in mother (n=1, 1.6%), 46 XX DSD with no diagnosis (n=2, 3.2%) and ovotesticular 46 XX DSD (n=1, 1.6%) diagnoses were included.
In the 46 XY DSD group, partial gonadal dysgenesis (n=5, 8.1%), complete gonadal dysgenesis (n=5, 8.1%), androgen synthesis defects (n=17, 27.4%), partial androgen insensitivity syndrome (n=2, 3.2%), complete androgen insensitivity syndrome (n=3, 4.8%), persistent muller canal syndrome (n=3, 4.8%) and 46 XY with no diagnosis (n=3, 4.8%) were included.
There was no significant difference between 46 XX DSD and 46 XY DSD groups **in** both child and parent Total PedsQL scores. In the subscale scores, the PedsQL Physical Functionality Score (PFS) filled by children was significantly lower in the 46 XX DSD group than in the 46 XY DSD group (p=0.01).
When the relationship between the sex in which the child was raised and the quality of life scores was evaluated; no significant difference was found in both child and parent scores (p>0.05).
There was mental illness in the family in 8.1% (n = 5) of the cases. There was no significant relationship between mental illness in the family and QoL scores of the children and parents (p >0.05).
Forty nine (79.0%) patients had surgical intervention and 13 (21.0%) had no surgical intervention. Surgical interventions were examination, corrective operation and gonadectomy.
The QoL PFS filled by children was significantly higher in patients with surgical intervention than those without (p=0.039).
In our study 72.6% (n = 45) of the cases were prepubertal and 27.4% (n = 17) were pubertal. No sexually active case was detected. When looking at the QoL scores of the cases according to their pubertal status; No significant difference was found between prepubertal and pubertal cases in terms of QoL scores in the scales completed by children. PedsQL Emotional Functionality Score (p = 0.029) and PedsQL School Functionality scores (p = 0.003), among the QoL subscale scores completed by the parents, were found to be significantly lower in pubertal cases than in prepubertal cases.
Table 3 and Table 4 show the relationship between children's and parent's PedsQL scores and socio-demographic characteristics, endocrine groups, pubertal status and surgical intervention.
No significant correlation was found between endocrine diagnosis age (3.23 ±4.30 years), disease duration calculated from age of diagnosis (6.79 ±4.19 years) and PedsQL scores (p>0.05, Spearman Correlation Test).
When the relationship between age period and QoL was examined, no significant correlation was found between age and QoL scores completed by the children. In the parental scores, it was found that PedsQL total score (p = 0.012) and PedsQL school functionality (p <0.05) scores decreased with increasing age and there was a significant negative correlation between them (Spearman Correlation Test).
Hormone replacement therapy use was detected in 29% (n = 18) of the cases. No significant difference was found between those using hormone replacement therapy and those not using hormone replacement therapy in both child and parent QoL scores (p> 0.05, Mann-Whitney U Test).
Considering the scale scores between the two most common endocrine diagnostic groups, Congenital Adrenal Hyperplasia (CAH) and Androgen Synthesis Defects (ASD), the PedsQL PFS filled by children was significantly lower in patients with CAH than those with ASD (p = 0.017).
When the SDQ scores were analyzed, the SDQ behavioral total difficulty score filled by children was found to be significantly higher in the 46 XY DSD group than the 46 XX DSD group (p = 0.002).
SDQ Behavioral Total Score filled by children was found to be significantly lower in CAH than ASD (p = 0.027). In SDQ, filled by parents, Behavioral Total Score was found to be significantly higher in CAH than in ASD (p = 0.010). According to the SDQ scale filled by teachers, Emotional Total Score was found to be significantly higher in CAH than ASD (p = 0.042).
The Relationship Between Psychiatric Diagnosis, PedsQL And SDQ Scores:
PedsQL School Functionality Score filled by children and adolescents in the group with psychiatric diagnosis was significantly lower than the group without psychiatric diagnosis (p = 0.018).
In the group with psychiatric diagnosis, the PedsQL Total Score, PedsQL **Emotional** Functionality Score, PedsQL Social Functionality Score, Peds QL School Functionality scores **filled by parents** were significantly lower than the group that did not have a psychiatric diagnosis (p = 0.002, p = 0.005, p = 0.001, p = 0.001).
In the group with psychiatric diagnosis, SDQ total difficulty score filled by teachers and parents was significantly higher than the group without psychiatric diagnosis (teacher p = 0.001, parent p = 0.029). Table 5 shows the relationship between psychiatric diagnosis, PedsQL and SDQ scores.
Psychiatric disorders were detected in 22.2% (n = 10) of our prepubertal cases and in 35.3% (n = 6) of our pubertal cases. There was no significant difference between pubertal status and presence of psychiatric diagnosis (p >0.05, chi-square test).
DISCUSSION
Most studies on DSD focus on children's sex development and psychosocial well-being, sexual orientation and adult life. In the literature, the results of quality of life in children and adolescents with DSD were different (21). In one study,

psychological well-being and quality of life were not impaired in prepubertal children with DSD (22). In our study, no significant difference was found in terms of QoL scores between prepubertal and pubertal cases in the scales completed by children. However, PedsQL Emotional Functionality Score and PedsQL School Functionality scores, which are the scores of QoL subscale completed by the parents, were found to be significantly lower in pubertal cases compared to prepubertal cases. In another study, it was reported that there is an increased risk for emotional problems in children and adolescents with DSD (23). In the results of studies with adults with DSD, although some studies have reported psychological, functional and sexual disorders (24, 25, 26), others have not confirmed severe restrictions or psychological problems (27, 28).

Psychosexual outcomes and quality of life in DSD have been most extensively studied in CAH, which accounts for about half of DSD cases. According to Kuhnle et al., long-term effects on general HRQOL are not expected in CAH (29). Johannsen et al., have identified lower quality of life and more psychiatric symptoms in adult Danish women with CAH (25). Nordenskjöld et al. reported that both mutation type and surgical procedure affect long-term quality of life for women with CAH (24). In a study involving both male and female CAH patients, both reported much lower scores in quality of life than in the general population. The authors concluded that in both groups, poor hormone replacement therapy, obesity and sexual dysfunction may be responsible for impaired quality of life (30). Children with 46, XY DSD were less studied. Physical well-being is reported to be in most cases not different from the general population; however, conditions-specific effects on gender identity or self-perception have been described in adolescents (21).

Most of the DSD QL studies in the literature focused on CAH and female raised and adult cases (24, 25). As well as we know, our study is the first study evaluating QoL in Turkey by the way of comparing both 46 XX and 46XY DSD. In their study conducted in Finland, Jaaskelainen et al. found that QoL scores in cases with CAH (16 women and 16 men) were better than the control group (31).

In their cohort studies between female social gender and male social gender DSD patients in Brazil, Amaral et al., found that the adulthood quality of life in DSD patients was good in both genders. However, they found that male social gender DSD patients with 46 XX and 46 XY had better scores in the psychological domain than female social gender DSD patients (8). When looking at QoL studies in children and adolescents with DSD, in their studies on 60 adolescents aged 13-16, Kleinemeier et al. found that general psychological well-being was not affected (21). In their study, Jürgensen et al. reported that children aged 8 to 12 years with DSD had significantly lower scores in their own filled HRQOL than those without DSD. Especially HRQOL's self-esteem, physical health and school functionality dimensions were significantly lower. Comparison of HRQOL between the diagnostic endocrine groups revealed no significant group differences (22).

In our study PedsQL Physical Functionality Score filled by children was found to be significantly lower in patients with CAH than those with ASD. Considering that most cases with CAH have XX karyotype and all cases with ASD have XY karyotype, this finding may be attributed to gender difference. In addition, it was observed that the Quality of Life Physical Functioning subscale scores completed by the children were significantly lower in the 46 XX DSD group compared to the 46 XY DSD group. When evaluated together, it can be said that the quality of life of the cases with 46 XX DSD in our country who were raised in the female gender was lower. This finding is different from the findings of studies (8, 31, 21, 22) conducted in other countries in which both genders and endocrine groups were compared. It is important in terms of being the first data specific to Turkey.

In a research conducted in Netherlands, the scores of quality of life reported by the parents were not impaired in any dimension **(32).** Similarly, in our study, no significant difference was found between the two endocrine groups in the parental total and subscale PedsQL scores. **The fact that information about the quality of life was obtained from both cases and parents is strength of our study.**

In our study, when the relationship between age period and QoL was examined, no significant correlation was found between age and QoL scores completed by the children. However in the parental scores, it was found that PedsQL total score and PedsQL school functionality scores decreased with increasing age and there was a significant negative correlation between them.

In the research of Jürgensen et al. **(22)**, the differences between the scores of children and parents, especially in terms of self-esteem, psychological and physical well-being, have been previously described for other chronic diseases **(33, 34).** This study and the other similar studies emphasize the need for self-reporting in volunteer children who can report on themselves.

In the research of Jürgensen et al., variables such as gender identity / gender dysphoria, gender role behavior, genital surgery status of the child, number and timing of surgery or diagnosis subgroups, knowledge of the child about the current diagnosis were not associated with decreased quality of life **(22).** In our study, it was found that variables such as endocrine diagnosis age, disease duration, education status of the mother, gender in which the child was raised did not affect the quality of life. **In the QoL scores completed by the parents, it was determined that the PedsQL Physical Functionality Score increased significantly as the education level of the father increased. It is thought that this situation may be related with the increase in understanding and coping skills as the education level increases.**

In the study of Crawford **(35)** et al., lower HRQOL was reported in patients with DSD who underwent surgery. In the research of Jürgensen et al., no relation was found between genital surgery and HRQOL **(22).** However, in our study, the PedsQL PFS filled by children was significantly higher in those with surgical intervention than those without.

Ege University Faculty of Medicine DSD multidisciplinary team consists of pediatric endocrinology, pediatric surgery, genetics, child and adolescent psychiatry specialists. The team meets every month and discusses the patients followed up with the diagnosis of DSD and organizes follow-up and treatment. Multidisciplinary team meetings are held to ensure that the intervention in DSD cases is performed at the most appropriate time and condition. It was thought that higher the PedsQL PFS in our patients who underwent surgery might be related to this. In the studies of Miegon et al., thirty nine, 46 XY DSD case were evaluated for the long-term medical and surgical results using questionnare and semi-structured interview. They concluded that most of the participants were satisfied with their body image and that there was no difference in satisfaction with their sexual functions among men and women. The authors concluded that the assignment to either sex would lead to a successful long-term outcome in most 46, XY individuals with severe genital uncertainty **(28).**

In our study, psychiatric diagnosis was found in 16 (25.8%) cases. Children and adolescents with DSD are at risk due to the

difficult processes they have experienced from birth, so psychiatric evaluation is required. According to a research by Ozbaran et al. **(36),** ADHD, depression and anxiety disorder were found in DSD as psychiatric diagnoses. In the study of Jürgensen et al., it was found that the mental health of adolescents with DSD was not affected compared to the adolescents in the control group **(22).** In previous studies on CAH patients, it has been reported that anxiety disorder and ADHD are frequently seen in these cases **(37).** Studies on stress and quality of life levels of CAH patients show that these patients are under emotional stress that can cause depression and anxiety disorders **(25).** In our study the most common psychiatric diagnosis was ADHD (n = 13, 21.0%). This rate is higher than the prevalence of ADHD (3.4%) reported by Polanzyck et al. in the meta-analysis **(38). In a study assessing the prevalence of childhood psychopathology in Turkey, mental disorder prevalence was detected 17.1%, ADHD prevalence was detected 12.4% (39). The values in our study were higher for both disorders (respectively, 25.8%, 21%).**

The incidence of psychiatric disorders varies according to the age period and psychiatric diagnosis. While the rates of depression and some anxiety disorders (social phobia, panic disorder) increase with adolescence, the rates of some disorders such as ADHD and separation anxiety disorder decrease (40). In our study, the mean age of patients with psychiatric disorders was 11 (± 4.02) years, and the most common diagnosis was ADHD and Depressive Disorder.

In the research of Şan and his friends in our country; Physical health total score, psychosocial health total score and scale total score filled by parents and children were found to be statistically significantly lower in the ADHD group compared to the control group **(41).** In literature studies, it has been reported that the areas of psychosocial, academic and family functionality are the most affected in children diagnosed with ADHD **(42).**

In our study results, PedsQL School Functionality Score, which is filled by children and adolescents, is significantly lower in the group with a psychiatric diagnosis (the most common diagnosis is ADHD) compared to the group without a psychiatric diagnosis. In addition, PedsQL Total Score, PedsQL Emotional Functionality Score, PedsQL Social Functionality Score, PedsQL School Functionality Score filled by parents in the group with psychiatric diagnosis are significantly lower than the group without psychiatric diagnosis.

In the research of Sawyer et al., it was reported that children with psychiatric disorder had much worse HRQOL than children without psychiatric disorder in many areas. It has been reported in many areas that they have a worse HRQL than children with physical disorders **(43).**

Conclusions:

Considering our results, it is seen that psychiatric disorders in patients with DSD are the most important factor affecting the quality of life. When the literature is evaluated, no study investigating the effect of psychiatric disorder on quality of life in DSD patients in our country has been found. Therefore, our study is important to emphasize that psychiatric illnesses in DSD patients negatively affect the quality of life.

Consequently, the importance of psychiatric support and consultancy of a multidisciplinary team is very clear, especially for children and families. Further studies will be important to demonstrate whether multidisciplinary team collaboration and psychiatric support have a positive effect on HRQOL in individuals with DSD.

In Turkey, it can be said that the quality of life is lower in patients with 46 XX DSD who were raised in female gender. This finding is different from the findings of studies conducted in other countries in which both genders were compared. As in many countries, it is a fact that women in our country are exposed to more risk factors than men, starting from intrauterine life, during childhood, adolescence, adulthood and old age. Future studies with larger samples and control groups will shed light on this issue.

Strengths and Limitations:

One of the strengths of our study is that we evaluate psychiatric disorders through a semi-structured interview. **The fact that information about the quality of life was obtained from both cases and parents is another strength of our study.** Our study is important to emphasize that psychiatric diseases in DSD patients negatively affect the quality of life. The biggest limitation of our study is that the sample size is relatively small and there is no control group**. Our other limitation is that the teacher form of the SDQ questionnaire has no Turkish validity and reliability.**

Clinical severity of psychiatric illness and the presence of side effects related to drugs were not evaluated in this study, and this is another limitation of our study.

Author contributions: Birsen Şentürk Pilan was involved in protocol development, data collection, data analysis, coordination of the study, and manuscript writing. Burcu Özbaran was involved in protocol development, data collection, coordination of the study, and manuscript editing. Didem Çelik was involved in data collection. Tuğçe Özcan was involved in data collection and manuscript writing. Samim Özen was involved in data collection and manuscript editing. Damla Gökşen, İbrahim Ulman, Ali Avanoğlu, Sibel Tiryaki, Hüseyin Onay, Özgür Çoğulu, Ferda Özkınay, and Şükran Darcan were involved in data collection. All authors discussed the results and contributed to the final manuscript.

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Table 1- The Sociodemographic Characteristics:

Mean Age (Year)	***9.70 (±4.18)***
Gender of Rearing	**N (Percent)**
○ *Female*	36 (58.1%)
○ *Male*	26 (41.9%)
Education	**N**
○ *Not Yet In School*	19 (30.6%)
○ *Kindergarten*	2 (3.2%)
○ *Elementary Education*	34 (54.9%)
○ *High Shool*	7 (11.3%)
Age Of Mother (Year)	***34.83 (±6.72)***
Education Level Of Mother	**N**
○ *Primary School*	39 (62.9%)
○ *High School*	10 (16.1%)
○ *University*	7 (11.3%)
○ *Illiterate*	6 (9.7%)
Mental Illness in Mother	**N**
○ *Yes*	3 (4.8%)
○ *No*	59 (95.2%)
Physical Illness in Mother	**N**
○ *Yes*	8 (12.9%)
○ *No*	54(87.1%)
Age Of Father (Year)	***38.16 (±7.01)***
Education Level Of Father	**N**
○ *Primary School*	27 (43.6%)
○ *High School*	25 (40.3%)
○ *University*	9 (14.5%)
○ *Illiterate*	1 (1.6%)
Mental Illness in Father	**N**
○ *Yes*	2 (3.2%)
○ *No*	60 (96.8%)
Physical Illness in Father	**N**
○ *Yes*	6 (9.7%)
○ *No*	56 (90.3 %)
Consanguinity Between Parents	
○ *Yes*	**N**
○ *No*	22 (35.5%)
	40 (64.5%)

Table 2- Endocrine Diagnoses

Karyotipe	Endocrine Diagnoses	N/Rate	Gender Of Rearing F/M
46 XY DSD (Disorders of Sex Development)	Complete Gonadal Dysgenesis (CGD)	5 (8.1%)	5F
	Partial Gonadal Dysgenesis (PGD)	5 (8.1%)	5M
	Androgen Synthesis Defects (ASD) (LHRH gene, SLOS, StAR, CYP11A1, HSD3B2, HSD17B3, POR, SRD5A2)	17(27.4%)	11F/6M
	Complete Androgen Insensitivity Syndrome (CAIS)	3 (4.8%)	2F/1M
	Partial Androgen Insensitivity Syndrome (PAIS)	2 (3.2%)	2M
	Persistent Mullerian Canal Syndrome	3 (4.8%)	3M
	No diagnosis 46 XY DSD	3 (4.8%)	2F/1M
	46 XY Syndromic Kloaka Robinow etc.	4 (6.5%)	4M
46 XX DSD (Disorders of Sex Development)	Ovotesticular DSD	1 (1.6%)	1M
	Congenital Adrenal Hyperplasia (CAH)	15(24.2%)	13F/2M
	Virilizing Tumor Luteoma in Mother	1 (1.6%)	1F
	No diagnosis 46 XX DSD	2 (3.2%)	1F/1M
Sex Chromosome Disorders	45,XO / 46,XY(Mixed Gonadal Dysgenesis)	1(1.6%)	1F

Table 3: Relationship Between Children's PedsQL Scores And Sociodemographic Characteristics, Endocrine Groups, Pubertal Status and Surgical Intervention.

Sociodemographic Characteristics	PedsQL Subscale Median (Min-Max)				
	Physical Functionality	Emotional Functionality	Social Funcitonality	School Funcitonality	Total PedsQL Score
Gender of Rearing					
Female	76.56(34.38-100)	82.5(30-100)	97.5(45-100)	77.5(10-100)	81.52(35.86-97.83)
Male	84.37(68.75-100)	80(30-100)	95(60-100)	77.5(45-100)	82.06(57.61-96.74)
p-value	0.062	0.837	0.955	0.530	0.561
Mother's Education					
<8years	84.37(34.38-100)	87.5(30-100)	95(45-100)	80(10-95)	81.52(35.87-96.74)
>8years	75(50-100)	80(55-100)	100(60-100)	75(15-100)	80.43(35.86-97.83)
p-value	0.079	0.233	0.853	0.276	0.306
Father's Education					
<8years	84.37(34.38-100)	90(30-100)	95(45-100)	80(10-100)	83.69(35.87-96.74)
>8years	78.12(50-100)	80(30-100)	97.5(45-100)	75(15-95)	79.89(35.86-97.83)
p-value	0.213	0.105	0.546	0.272	0.298
Mental Illnes In The Family					
Yes	79.16(50-100)	86.2(55-100)	91.25(65-100)	67.5(15-90)	79.88(35.86-97.83)
No	79.72(34.38-100)	80.8(30-100)	88.6(45-100)	72.32(10-100)	80.1(35.87-96.74)
p-value	0.831	0.365	0.464	0.673	0.268
Endocrine Groups					
46 XX DSD	68.7(50-100)	80(55-100)	92,5(45-100)	80(15-90)	78.80(35.86-97)
46XY DSD	85.93(34.38-100)	82.50(30-100)	100(45-100)	77.50(10-100)	81.52(35.87-95.65)
p-value	**0.018**	0.476	0.381	0.932	0.509
Pubertal Status					
Prepubertal	79.5(56.25-100)	82(30-100)	89.51(55-100)	75(45-100)	81.23(57.61-96.74)
Pubertal	79.96(34.38-100)	80(30-100)	87.64(45-100)	66.47(10-90)	78.06(35.86-97.83)
p-value	0.482	0.966	0.655	0.410	0.657
Surgical İntervention					
Yes	84.37(34.38-100)	85(30-100)	100(45-100)	80(10-95)	82.60(35.87-97.83)
No	75(50-93.75)	80(55-100)	85(55-100)	75(15-100)	78.26(35.86-95.65)
p-value	**0.039**	0.391	0.097	0.945	0.193

Table 4: Relationship Between Parent's PedsQL Scores And Sociodemographic Characteristics, Endocrine Groups, Pubertal Status and Surgical Intervention

Sociodemographic Characteristics	PedsQL Subscale Median (Min-Max)				
	Physical Functionality	Emotional Functionality	Social Funcitonality	School Funcitonality	Total PedsQL Score
Gender of Rearing					
Female	78.12(31.25-100)	85(30-100)	100(10-100)	80(35-100)	83.69(44.57-98.91)
Male	71.87(21.88-100)	80(30-100)	85(20-100)	80(30-100)	76.08(51.09-100)
p-value	0.158	0.590	0.087	0.815	0.090
Mother's Education					
<8years	78.12(21.88-100)	85(30-100)	100(10-100)	80(40-100)	82.60(44.57-98.91)
>8years	78.12(31.25-100)	80(30-100)	85(20-100)	80(30-100)	78.26(46.73-100)
p-value	0.792	0.464	0.142	0.324	0.613
Father's Education					
<8years	71.87(21.88-100)	85(30-100)	90(10-100)	80(30-100)	78.26(44.57-98.91)
>8years	78.12(31.25-100)	85(30-100)	100(20-100)	80(35-100)	81.52(46.73-100)
p-value	**0.043**	0.754	0.183	0.802	0.311
Mental Illnes In The Family					
Yes	75(31.25-100)	71(45-95)	68(20-100)	59(30-90)	71.30(46.73-96.74)
No	74.21(21.88-100)	80.7(30-100)	86.14(10-100)	17.8(40-100)	13.71(44.57-100)
p-value	0.683	0.291	0.784	0.092	0.475
Endocrine Groups					
46 XX DSD	78.12(31.25-100)	85(30-100)	95(20-100)	80(35-100)	79.89(46.73-96.74)
46XY DSD	78.12(21.88-100)	80(30-100)	100(10-100)	80(30-100)	82.06(44.57-100)
p-value	0.587	0.751	0.401	0.758	0.896
Pubertal Status					
Prepubertal	74.92(21.88-100)	83(30-100)	86.77(20-100)	81.71(30-100)	81.11(51.09-100)
Pubertal	72.61(31.25-100)	71.8(35-100)	79.1(10-100)	65(35-95)	78.06(35.86-97.83)
p-value	0.735	**0.029**	0.540	**0.003**	0.074
Surgical İntervention					
Yes	76.56(21.88-100)	85(30-100)	95(10-100)	80(40-100)	80.43(44.57-80.43)
No	81.25(31.25-100)	80(30-100)	85(20-100)	85(30-100)	84.78(46.73-97.83)
p-value	0.327	0.721	0.330	0.932	0.885

Tablo 5- Relationship Between Psychiatric Diagnosis, PedsQL and SDQ Scores:

PedsQL Subscales	Without Psychiatric Diagnsosis			Having Psychiatric Diagnosis			
Children	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**	**P**
Physical Functionality	**82.81**	34.38	100.00	**78.12**	50.00	100.00	0.160
Emotional Functionality	**85.00**	55.00	100.00	**80.00**	30.00	100.00	0.385
Social Functionality	**100.00**	45.00	100.00	**90.00**	45.00	100.00	0.056
School Functionality	**80.00**	45.00	100.00	**65.00**	10.00	95.00	**0.018**
Psychosocial Functionalityy	**86.66**	58.33	98.33	**73.33**	28.33	96.67	0.090
Total PedsQL Score	**83.69**	58.70	97.83	**77.17**	35.86	96.74	0.056
Parent	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**	**P**
Physical Functionality	**78.12**	21.88	100.00	**78.12**	21.88	100.00	0.912
Emotional Functionality	**90.00**	30.00	100.00	**65.00**	30.00	100.00	**0.005**
Social Functionality	**100.00**	35.00	100.00	**80.00**	10.00	100.00	**0.001**
School Functionality	**85.00**	40.00	100.00	**60.00**	30.00	100.00	**0.001**
Psychosocial Functionality	**90.00**	45.00	100.00	**68.33**	36.11	100.00	**0.000**
Total PedsQL Score	**84.78**	51.09	100.00	**66.30**	44.57	100.00	**0.002**

SDQ	Having Psychiatric Diagnosis			Without Psychiatric Diagnsosis			
Children	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**	**P**
Emotional symptoms	**2**	0	5	**3**	0	7	0.145
Hyperactivity/inattention	**3**	2	7	**3**	0	7	0.502
Conduct problems	**2**	0	3	**2**	0	5	0.469
Peer relationship problems	**2**	1	5	**2**	0	7	0.274
Pro-social behavior	**9,5**	8	10	**9**	7	10	0.614
Total Difficulty Score	**11**	6	19	**9**	2	16	0.096
Parent	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**	**P**
Emotional symptoms	**1**	0	7	**2**	0	6	0.305
Hyperactivity/inattention	**5**	0	9	**3**	0	7	**0.010**
Conduct problems	**1**	0	8	**1**	0	5	0.231
Peer relationship problems	**2**	0	6	**2**	0	6	0.936
Pro-social behavior	**8**	4	10	**8**	3	10	0.252
Total Difficulty Score	**10**	1	24	**7**	1	21	**0.029**
Teacher	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**	**P**
Emotional symptoms	**2**	0	6	**1**	0	5	0.101
Hyperactivity/inattention	**6**	0	9	**2**	0	7	**0.002**
Conduct problems	**1**	0	9	**0**	0	4	0.051
Peer relationship problems	**4**	0	7	**1**	0	6	**0.004**
Pro-social behavior	**8**	0	10	**9**	4	10	0.180
Total Difficulty Score	**13.5**	0	29	**5**	0	16	**0.001**