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Psychological distress in children with Disorders of Sex Development.

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Abstract

Children with 46XY disorders of sex development with genital ambiguity face a lot of behavioral changes and are associated with many risk factors. The 20 participants (aged 5-16) were taken, consisting of 12 boys and 8 girls. Control data were obtained from a representative sibling of each patient who was matched for age and gender. A questionnaire was held which was parent administered to check the behavior of child. The analysis came out to be that the children with genital ambiguity have poorer scores in respect to social or other realms when compared with control group. These findings are helpful as they give a chance to understand the individuals with any genital ambiguity and it should become an integral part to counsel them psychologically.

Introduction

Disorders of sex development (DSD) are defined as congenital conditions in which the development of chromosomal, gonadal, and anatomic sex is atypical [1]. These disorders are a heterogeneous group of rare conditions. It has been estimated that the incidence of patients presenting with ambiguous genitalia at birth is approximately 1 in 4500– 5500 [2, 3]. Numerous hormonal treatments, surgery, long term follow up are done to these individuals to help them lead a normal life. All these may result into distress or some kind of depression. Among those with 46XY DSD, the largest group studied was found to be of partial androgen insensitivity syndrome (PAIS). A long-term follow-up study of adults with PAIS show that there is increased psychological distress in this group. In female it mainly occurs due to deficiency of 5-alpha reductase and 17-beta hydroxyprogesterone. Outcomes of mental health results in depression, suicidal attempts, self-harming behavior. The management of DSD is very complex and has undergone major shifts. The initial approach was to apply only gender policy. But after reviewing some reports and recommendations it was advised to first take the consent of patient and his/her parents fully, and then only further procedure to be done. It is thus imperative to assess psychological outcomes of these patients to allow for evaluation of management policies which can then guide future clinical practice guidelines. To this end, in this study, we assessed the behavioral problems of children with 46XY DSD with genital ambiguity. Patients were recruited from Sir Sunderlal Hospital, Banaras Hindu University, Varanasi.

2. Research Objective

The general objective of this study was to evaluate the behavioral problems of patients with 46XY DSD with genital ambiguity and to identify any risk factors that may influence behavior.

3. Methods and Study Design

3.1. Study Outline. The study was carried out from 18 January 2020 to December 2020. The samples were collected from Department of Pediatrics, Sir Sunderlal Hospital, Banaras Hindu University, Varanasi. All patients with 46XY DSD with genital ambiguity aged 5–16 years (N = 20) who attended the pediatric clinic at SSH were invited to participate in the study. Of those, patients with syndromes, learning disabilities, and neurologic disorders were excluded from the study. Patients who did not attend the follow-up despite reminders were also excluded. The median age of this group was 11.5 (7.8–13.3) years, significantly lower than the patient group. Therefore, a total of 20 patients were included in the study: male social sex N = 12 and female social sex N = 8. All the controls came from the families of cases (N = 20, males = 12, females = 8), and only one sibling from the family closest to the case's age was chosen. The patients were identified from clinic records. Written informed consent was obtained from the parents (or legal guardians) of all the patients during a clinic visit before participation. After obtaining informed consent, a self-administered questionnaire was distributed to the parents. Approval for the study was granted by the ethical committee of Institute of Medical Sciences, BHU.

All the clinical data was collected and obtained from each individual's medical reports and gender assigned, clinical and other biochemical data, degree of virilization, nature of surgeries done, pubertal status was also obtained. Further karyotyping was also done. Other data like medication, socioeconomic data and any other type of complications related information was also collected during the time of interview. To group the patients, classification was done on basis of karyotyping, sex rearing or recent sex of the individual.

Background clinical data were obtained from medical records and included age at diagnosis, karyotype, gender assigned, clinical and biochemical data at presentation including degree of virilization, number and nature of surgical procedures done, and pubertal status. Current information about the patients including pubertal development, complications, medication, and socioeconomic data were obtained by physical examination and interview at the respective clinic. To group the patients, we applied a classification system based on karyotype and sex of rearing/recent gender. Two subgroups were made as follows: (a) Subgroup 1 (XY-F, N = 8): individuals with XY karyotype and reared as girls/living as women (b) Subgroup 2 (XY-M, N = 12): individuals with XY karyotype and reared as boys/living as men.

3.2. Questionnaire. The study tool was based on the behavior of child. The proxy version of this tool was used, that is, the parents answered the questionnaire. This study tool consists of a large number of questions which were answered by the parents. The parents answered the questions based on the child's behavior over a 6-month period. Parents rated their child's demonstration of behavior by scoring 0 for never, 1 for sometimes, and 2 for always. The behavioral problem scales are derived from various combinations of the items or questions. The questionnaire provides three summary scales and eight syndrome scales.

4. Results

4.1. Patient Cohort and Control. There was no significant difference between the patient and control groups with regard to age, gender distribution, mean family income, and parental marital status (Table 1). Similarly, there was no difference between male and female patients as compared to male and female controls with regard to demographic characteristics. Patient characteristics are summarized in Tables 1, 2, and 3. The median age of the population was 14 years (12–15). Twelve patients were included in the group XY-M with a median age of 13 years (10–15), and 8 patients were included in the group XY-F with a median age of 14.5 years (10.8–14). There was no statistical significance between the ages of the two groups. 12 patients (60%) were adolescents (above 11 years old). The majority of patients had already had some surgical procedure, with 9 patients having undergone a genital reconstruction. Eight patients had three or more surgical procedures. Nine patients had had a gonadectomy, in seven cases bilateral. Two patients had a gonad blastoma at the time of removal of gonads. One patient with Ovo testicular DSD underwent gender change from female to male. Analysis of syndromic scale scores revealed that the patient group had significantly poorer scores in the anxious depressed, social, and rule-breaking dimensions the XY-F group had higher scores (more pathological) than the XY-M groups, although the difference was not statistically significant. Prevalence of DSD Patients with Clinical Range Scores. A chi-square test of independence was performed to examine the proportion of DSD cases with clinical range scores as compared to the controls.

Table 1: Sociodemographic characteristics of cases and control.

Variable	Case	Control	P value
Median age at study entry in years (IQR)a	12 (3)	11 (3)	0.32
Gender frequency (%) b			0.70
Male	20 (76.8)	19 (73.1)	
Female	5(21.2)	6 (24.9)	
Mean family income RM (SD)c	3850 (1333)	4000 (1486)	0.69
Parental marital status			
Married	25	25	1.00
Single	1	1	

aMann–Whitney; bchi-squared test; cindependent t-test; dFisher's exact test.

Table 2: Baseline characteristics of DSD cases.

	Male (*N* = 12)	Female (*N* = 8)

Age in years at study entrya	12.5 (3.6)	14 (2.7)
Prader scoreb		
2		2 (27)
3	2 (8)	4 (71)
4	12 (65)	
5	5(26)	
Surgical proceduresb	16 (76.3)	5 (83.1)
Number of surgical procedures		
≤2	8	3
>2	7	1
Gonadectomy	4	4
a Mean (standard deviation); frequency (%).		

Table 3: Chart showing the grouping of patients and the distribution of diagnosis.

Group		**Group**		
Total		**XY-M**	**XY-F**	
Diagnosis	Gonadal dysgenesis	6	0	6
	Mixed gonadal dysgenesis	2	3	5
	Androgen insensitivity	1	5	6
	Ovotestis	2	0	2
	5-alpha reductase deficiency	1	0	1
Total		12	8	20

Table 4: Syndrome scale T scores in patients with XY DSD ascompared to the control group.

	Case	Control	P value

Anxious-depressed*	52 (8)	50 (1)	0.003
Withdrawn-depressed	52 (12)	50 (0)	0.006
Somatic problems	50 (8)	50 (3)	0.286
Social*	54 (13)	50 (3)	0.001
Thought	50 (5)	50 (0)	0.008
Attention	52(9)	50 (1)	0.038
Rule-breaking*	52 (10)	50 (1)	0.004
Aggressive	50 (7)	50 (1)	0.095
**** denotes significant variables. Scores are given as median (IQR) withhigher scores denoting poorer outcome. P value was adjusted using theBonferroni-Holm method to account for multiple comparisons.***			

Discussion

It was found in the study that the individuals with genital ambiguity experienced behavioral problems as compared to control group. In respect of social, anxious depressed and rule breaking - all kind of realms, the analysis of the behavioral scores of patients' group was poorer when compared to control group. The patients were psychologically disturbed when compared to control group. Various outcomes are seen in individuals with DSD like they have a greater risk of behavioral problems and poor psychological behavior. As they encounter societal hurdles and pressure so are likely to have negative psychological implications. They may get psychologically disturbed if are exposed to repeated surgery and medical intervention. Sometimes they are forced to adjust with these limitations. Individuals with DSD are more prone to psychological distress as the society doesn't accept them as they see them as an added burden on society. Individuals with any genital ambiguity usually remain isolated and this stigma is responsible for their psychological behavior problems. The greatest degree of psychological distress would be found in the groups where there was a discrepancy between the genetic and social sex. The authors postulated that this may be either as a direct consequence of androgen effects or as a more indirect consequence of a feeling of "being different" caused by atypical physical and/ or behavioralcharacteristics. The rarity and complexity of this group often leads to a delay in diagnosis and also to a delay in accessing specialized medical care. Thus, this may be a group that needs greater surveillance and psychological support. The gender of rearing and socialization also play a role in gender identity development. Thus, for this group of patients, parenting and social relationships are of paramount importance and the patients and their families should receive appropriate support throughout the patient's development phase. Family dynamics and parenting heavily influence the psychological outcomes of a child. This will also help in identification of families who are at high risk. Medical practitioner's attitude also influences the psychological aspects of disorder management of DSD. In summary, this study demonstrated that children and adolescents with DSD have a higher degree of psychological distress. It is recommended by current findings that psychologicalcounseling should be an integral part of the professional support offered to patients with

DSD. It should also be recommended that people in the society do not consider them as an added burden and help them to not to feel distress. The findings reported here also underline the importance of establishing pediatric mental health services to support the social and behavioral development of these patients.

Conflict of interest

Authors have declared that and research was conducted in and the absence of any commercial or financial relationships without any conflict of interest.

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Author Contributions
R.S., R., A. contributed to the conception, design, and writing of the study protocol and the design of search strategies; N.K.S., A K.Y., M.K. located and obtained reports, helped to select and assess cases, conducted the data analysis, and drafted and approved the final paper. All authors contributed to the conception, design, and writing of the study protocol, conducted data analysis and revised and approved the final paper.

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