Gender Identity shows a high correlation with Prader score in patients with disorders of sex development (DSD) presenting in mid childhood

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Abstract *Objective:* In developing countries like Bangladesh, delayed presentation for disorders of sex development (DSD) is common, and provides some special problems for management. There remains significant controversy about appropriate sex assignment in this group. We aimed, therefore, to assess gender identity (GI) in 50 consecutive patients with DSD presenting to a referral centre in Chittagong, Bangladesh, and correlate it with Prader score, to see if the latter could be used to predict GI. *Methods:* A cross-sectional, case-control study of 50 consecutive children with DSD and 50 children with vascular anomalies was conducted in the Pediatric Surgical Clinic, Chittagong Medical College & Hospital (CMCH). After informed consent, patients and controls provided oral answers to a GI questionnaire and had a detailed history and physical examination. Sex-typed activities were assessed by observations of a structured toy play and the child's selection of a toy to keep. Both patients and parents then completed the Child Game Participation Questionnaire (CGPQ). *Results:* There were no differences in age (2-16 years, mean 8.74) between controls and DSD patients (11 46,XX DSD, 32 46,XY DSD, 4 MGD, 3 ovo-testicular DSD). Fifteen of the DSD patients (30%) came from consanguineous marriages and only 2 of the control patients had consanguinity of their parents. For the 13-question GI interview, there was no overall difference between DSD cases and controls. For the 46,XX DSD subgroup, there was a significantly higher score (11.1 ± 7.1) compared with control girls (4.5 ± 4.7) ($p < 0.05$), while for DSD and control boys, there was a positive correlation with age and GI ($p < 0.01$). Prader score correlated with GI score in both control ($r=0.91$) and DSD patients ($r=0.75$) ($p < 0.01$), DSD girls played significantly less with girls' toys than controls ($p < 0.01$), but there was no differences for the boys. Composite scores on GI and gender-related behaviour correlated with Prader score for DSD patients ($r=0.61$) ($p < 0.01$). *Conclusion:* This study supports the view that GI and gender-role behaviour should be assessed routinely in DSD patients presenting after the neonatal period, so that sex assignment is in accordance with behaviour. Prader scores showed a good correlation with GI and gender role behaviour.

Key words – disorders of sex development [DSD]; mid –childhood ; Prader score ; gender identity

Introduction: Disorders of sex development (DSD) are congenital conditions in which development of chromosomal, gonadal or anatomical sex is atypical [1]. Though there has been progress in diagnosis, surgical techniques and understanding of psychological issues, many controversies remain in the diagnosis and management of DSD. Analysis of clinical management strategies has focused on gender assignment and the desirability and timing of genital surgery. The determinants of gender identity (GI), however, are much less known and most likely multiple, such as exposure to androgens, sex chromosomes and brain structure, as well as social and cultural circumstances and family dynamics [2]. Infants develop a sense of GI or self-definition as male or female in the first 2-3 years of life [3]. In developed countries, XX patients with ambiguous genitalia, usually caused by congenital adrenal hyperplasia (CAH), are raised as female but the situation becomes more complicated when the karyotype is also ambiguous with the presence of some Y material. It is in this group of “Y-deficient” patients that gender assignment is most difficult, and anatomical factors influence the final choice[1,2]. If early gender assignment is desirable, which is disputed by some, we still need criteria allowing us to predict the GI correctly. In a developing country like Bangladesh, there are other complicating factors, such as late diagnosis, often in mid childhood, and also a widespread fear in the society about ‘Hijra’ [4-8]. People with DSD, when they reach into their adulthood are termed as 'Hijra' in the subcontinent, who are a significant presence in the South Asian culture. They are alienated from family and society and get little sympathy from the society. Their story more closely resembles discrimination, harassment, malicious rumours, marginalization, dejection and denial of human rights; and they are compelled to earn their living by collecting money from shopkeepers, passengers and passersby –a form of mild extortion — and by crime and prostitution; thus run a higher risk of contracting and spreading AIDS and sexually transmitted diseases[4-6].

There is no published study of patients with DSD in Bangladesh, and few get specialised care, due to lack of expertise and a dedicated team for these patients. Multiple studies have shown that external virilisation is directly proportional to the amount of prenatal androgens [9,10]. This study aimed to

make an assessment of a child's GI gender-role behaviour, to see how this could assist in the process of sex assignment and also how it correlated with the degree of external virilisation in children presenting to Chittagong Medical College & Hospital (CMCH).

Methods: This was a cross-sectional, co-relational, case-control study carried out between January 2012 and December 2012, evaluating 50 consecutive patients with DSD and 50 with a vascular anomaly who presented to the Department of Pediatric Surgery, CMCH. Patients were included if they were between 2 and 16 years of age and the parents gave informed consent. Patients and controls were asked to provide oral answers about GI in a questionnaire **with the help of one of the authors and their parents** (Table 1). The questionnaire was composed of 13 questions on gender

Table 1

identity. Each question was scored on a 3-point scale ranging from 0 to 2. A 0 was assigned if the child answered a question which is normal for a girl. A 2 was assigned if the child answered a question which is normal for a boy. A 1 was assigned if the child provided an ambiguous response, **kept silent or could not answer** [11,12]. Boys and girls were labeled as they were raised by their parents. Activities and interests were assessed by observations of (i) sex-typed toy play; (ii) child's selection of a toy to keep; (iii) child self-report on the Child Game Participation Questionnaire (CGPQ); and (iv) Parent-report on the CGPQ [9,11,13,14]. Toy preference was measured by the amount of time the child played with 3 categories of toys: (i) Boy: cars, pistols, aeroplanes; (ii) Girls: dolls, doll clothing, kitchen supplies; (iii) Neutral: books, sketchbook, marker pens. Toys were arranged in a standard order in a semicircle on the floor in the play corner of the ward in an area approximately 15 x 8 feet, with every other toy being masculine or feminine and neutral toys in between. The child was asked to sit in the middle of the semicircle and was recorded for 10 minutes when playing. Play was defined as the child touching toy, and scoring was done by a person blinded to the child's gender status. A score of 1 was assigned for each minute of play with each category of toys and the score on play with boy's toys was compared. Because an observer was present during the toy preference situation, a child's toy choice may reflect knowledge of sex role stereotypes rather than true preference. Therefore, we asked the child to select a toy in private to keep, from a

bag containing a pistol, ball, book, marker pens and a doll; and scoring was done from 5 to 1 respectively.

Finally, children were asked to provide oral answers for their preferences for a variety of sex-typed activities and games. They were asked whether or not they liked each of the listed activities (Table 2). Each masculine play was assigned a score of 1 and total score on masculine play (out of 15) was

Table 2

compared. Parents also completed the CGPQ with the same type of scoring. A composite score was calculated by converting all the scores into a same denominator by taking a least common multiple and taking the means of the numerators after converting the numerators accordingly. The composite scores were then compared with the Prader score. A detailed history included age, apparent sex at birth, sex of rearing, socioeconomic status (according to World Bank common international poverty line, 2008), gestational age, birth weight, family history and relationship between parents. A detailed physical examination recorded the status of the genitals, secondary sex characteristics and whether or not there was facial dysmorphism, other anomalies or hyperpigmentation. Depending on the DSD status children had chromosomal, hormonal and metabolic tests, along with ultrasonography, urogenital sinugram, cystoscopy +/- laparoscopy. Some patients had gonadal biopsy. All data were collected on a predesigned collection sheet and analysis was done by standard statistical methods using SPSS17. Student's t test was used to compare the means of scores of ambiguous and deviant responses in GI interview and time of play in observed toy preferences. Pearson correlations were computed between age and GI score, Prader and GI score, Prader score and child's and parents report on CGPQ; and finally Prader and composite score.

Results: There were 35 children less than 5 years old, 41 between 5 and 10, and 24 more than 10 years old in both groups. There was no significant difference between DSD patients and controls with regards to age, apart from a slight preponderance of younger control patients. The DSD cohort contained 11 patients with 46,XX DSD (congenital adrenal hyperplasia: CAH), 32 with 46,XY DSD (5 partial androgen insensitivity syndrome, 2 primary testicular dysgenesis, two 5- α reductase

deficiency and others not specified), 4 with mixed gonadal dysgenesis (MGD) and 3 with ovotesticular DSD. Of the 50 DSD patients, 13 were reared as girls and 37 as boys. Fifteen (30%) were blood related, with 7 of these being first cousins (2 46,XX DSD and 5 46,XY DSD). In the GI interview, comparison of means of scores of ambiguous and deviant responses was done by student's t test. The means were 14.4 ± 9.1 for DSD patients and 11.6 ± 9.4 for the control group. The value of 't' was not significant, indicating that the DSD patients did not have significantly different responses from those of the control group (Fig. 1). When the 46,XX DSD patients (n=11) were examined separately, their score was 11.1 ± 7.1 , compared with 4.5 ± 4.7 in control girls ($p < 0.05$). Patients with 46,XY DSD scored the same as control boys. Pearson correlation showed that in both DSD and control girls, age was negatively correlated with GI score ($r = 0.72$, DSD; $r = 0.69$, control $p < 0.01$), indicating fewer deviant responses with age. For both DSD and control boys, GI score correlated positively with age ($r = 0.43$, DSD; $r = 0.69$, controls; $p < 0.01$) (Fig. 2). Two control girls and 1 DSD girl could not answer the questions which were interpreted as missing data and 2 girls in both groups had the same scores. One control boy and 1 DSD boy could not answer the questions and there were 5 similar scores in control boys and 3 in DSD boys.

Fig.1.

Fig.2

The Prader score positively correlated with GI score in both controls ($r = 0.91$) and DSD patients ($r = 0.75$) ($p < 0.01$) which means that with the increase in the masculinity of the genitalia, the masculinity scores of the gender identity also increased (Fig. 3). There were 3 missing data in control group and 2 in DSD group. In the control group 14 babies had similar scores at Prader 0 and 21 babies at Prader 5. In the DSD group 3 had similar scores at Prader 2, 6 at Prader 3, 19 at Prader 4. Girls with DSD played significantly less with girls' toys than controls (mean 3.5 minutes vs 6.2 minutes; $p < 0.01$), while there were no differences between the boys. Control girls were more likely to select a doll to keep (15/25) compared with DSD girls (3/13). On the CGPQ, DSD girls reported to play with boys' games more than control girls, and child self-report on the CGPQ correlated positively with Prader score in both controls ($r = 0.77$) and DSD patients ($r = 0.54$) ($p < 0.01$). Parent-

Fig. 3.

reported scores on CGPQ were similar to their children's report. The composite score of GI and gender-related behaviour correlated with the Prader score in DSD patients ($r=0.61$; $p<0.01$) (Fig. 4).

Fig. 4.

There were 2 missing data and 2 babies had similar scores at Prader 3 and 4.

Discussion: This study showed that 46,XX DSD patients, regardless of whether they were raised as boys or girls, had a significantly higher masculinity score than the control girls in the GI interview. In both the DSD and control girls, age negatively correlated with the GI scores, while in both boys (DSD + controls), age positively correlated with the GI scores, indicating that there were fewer deviant responses with age.

The Prader scale was originally designed to see the degree of virilisation of external genitalia in patients of CAH and later adopted for all DSD patients. It is a 6 point score starting from '0', which describes normal female external genitalia extending to '5', which describes normal male external genitalia. The Prader scale predicts the extent of exposure to androgens between 8 and 12 weeks of gestation. The greater the degree of virilisation, the greater is the amount of early androgen exposure and the greater the extent of vaginal regression [9]. In this study, Prader score positively correlated with GI score in both controls and DSD patients. DSD girls played significantly less with girls' toys than controls, and also reported to play more with boys' games. A composite measure of GI and gender-related behaviour correlated with the degree of genital virilisation measured by the Prader score. The role of prenatal hormones in determining GI has been studied at length, since a case report of a boy reassigned as a girl after a mishandled circumcision in infancy, but who experienced gender dysphoria and requested reassignment back a male in late childhood [2,16]. Age was negatively related with the number of deviant responses in the GI interview, as documented by others, consistent with children needing to achieve concrete operational thought before they can correctly classify their own gender [12]. Given the average age of the children in this study, it is possible that a number had not reached this level of maturation. Though infants develop a sense of GI or self-definition as male or female in the first 2-3 years of life, it was very difficult to extract it through the interview. There were 6 babies in this study who were below 3

years of age; no answer could be obtained from 2 and they were calculated as missing data. Other 4 babies provided answers to some of the questions with the help of their parents and those were consistent with their reared sex. The questions which they did not or could not answer were labeled a score of 1. The findings of masculine-typical play in 46,XX DSD girls are consistent with previous studies [15,17]. Some of our other findings emphasise the importance of adequate measurements. Although CAH girls had more boy-typical responses than control girls, the magnitude of differences varied across the tests, and was generally moderate. This study had some limitations, related to its cross-sectional design and lack of longitudinal data. The small sample size meant that we were unable to study patients with MGD or ovotesticular DSD separately. The questionnaire format may also have affected some of the responses because of poor levels of education and the hospital environment. Also the age range 2-16 years is very wide. Similar questionnaires may not be suitable for the whole group which may affect the common generalized conclusion, but it was very satisfactory especially for the delayed presenter group. Nevertheless, it forms a significant starting point for assessing DSD patients and their management in developing countries of South Asia. This will also help in the decision making steps of gender assignment of DSD patients where there are lack of Psychologists or Pediatric Psychiatrist to aid in the complete psychological assessment of these patients.

Conclusion

This study supports the view that GI and gender-role behaviour should be assessed routinely in DSD patients presenting after the neonatal period, which is common in developing countries, so that sex assignment is in accordance with behaviour and Prader score.

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Legends :

Table 1: Gender identity Questionnaire

Table 2: Child Game participation Questionnaire

Fig-1: Showing ambiguous and deviant responses of GI interview in both DSD and control groups.

Fig-2: Scatter diagram showing correlation between Age and GI score in both control and DSD girls and boys. (There were 2 missing data in control girls and 1 in DSD girls. Two girls in both groups had the same scores -9 years with GI score 0 in control girls and 7 years with GI score 7 in DSD girls.

There was 1 missing score in DSD boys and 1 in control boys. Three control boys of 5 years with GI score 23 and 2 with GI score 24, 2 of 8 years with GI score 25 and 2 of 12 years with GI score 24; 2 DSD boys of 5 years with GI score 21, 2 of 12 years with GI score 24 and 2 of 16 years with GI score 26)

Fig-3: Scatter diagram showing positive correlation between Prader score and GI score in both control and DSD groups. (There were 3 missing data in control group and 2 in DSD group. In the control group 6 babies with Prader score 0 had a GI score of 0, 4 had 1, 2 had 5 and 2 had a GI score of 7; and 3 control babies with Prader score 5 had a GI score of 20, 2 had 21, 2 had 22, 3 had 23, 6 had 24, 2 had 25 and 3 had 26. The similar scores in DSD group were 3 with a GI score 7 at Prader 2, 3 had 19 and 21 at Prader 3, 2 had 19, 4 had 21, 3 had 23, 3 had 24 and 7 had 26 at Prader 4.)

Fig-4: Scatter diagram showing correlation of composite score to Prader score

Fig-1