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DISORDERS OF SEXUAL DIFFERENTIATION AS SEEN AT KENYATTA NATIONAL HOSPITAL

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ABSTRACT

Background: Disorders of sexual differentiation (DSD) are a group of congenital anomalies characterised by discordance between genetic, gonadal and phenotypic sex. There has been remarkable evolution in management over the last decade, including nomenclature, diagnosis and management. There has also been increased awareness and interest from patients and the public, including legal opinion. There has however been no local study to document and evaluate management in Kenya.

Objective: To describe management of patients presenting with DSD at Kenyatta National Hospital (KNH) over a 10 year period.

Design: Retrospective descriptive study.

Setting: Kenyatta National Hospital.

Subjects: Patients diagnosed with DSD.

Results: A total of 30 patients whose charts were available were reviewed. Age ranged from birth to 19 years (median 5 months) at diagnosis. Presumed gender was assigned at birth in 28 patients. Karyotyping was available in 23(76%) patients. Other common tests included blood tests (23, 76%), ultrasound scan (14, 47%), contrast studies (3, 10%) and exploratory laparoscopy or laparotomy. 46XX and 46XY DSD were the most common conditions encountered (13, 43% and 7, 23% respectively). The commonest operations were correction of hypospadias and orchidopexy (55%), followed by feminising genitoplasty (16%). Only two patients had gender reassignment. Fifteen patients were asked how they feel about their current gender, and 11 expressed satisfaction.

Conclusion: DSD is a relatively rare condition. There are also no strict protocols being followed. Management at KNH is acceptable although there is a lack of facilities to carry out many requisite investigations.

INTRODUCTION

Disorders of sexual differentiation (DSD) are a spectrum of congenital anomalies with a common presentation pathway of disordered phenotypic expression of gender. In all these children, it is not easy to allocate a male or female gender at birth based on physical features alone. These disordered features include nonpalpable testes, micropenis, clitoromegally, hypospadias, posterior labial fusion and sex chromosome discordance. At times diagnosis is made late with primary amenorrhoea. The patient should then have serum electrolytes and adrenocortical hormone estimation. Thereafter, in order of convenience, various tests are carried out like ultrasound, laparoscopy, and gonadal biopsy and

karyotype studies. Classification of DSD currently depends on chromosomal make up, and this directly influences management (1, 2).

Nowadays, diagnosis is made faster and easier, and surgeons have mastered the art of genital reconstruction. The paradigm has however shifted from early surgical reconstruction to delayed intervention and gender reassignment, in spite of mandatory workup and diagnosis in neonatal period for purposes of gender assignment (2, 3).

Gender assignment is determined by the patient, relatives and the multidisciplinary team (4). It depends on molecular diagnosis, genital appearance, prenatal androgen exposure, surgical options, need for lifelong hormonal replacement, fertility potential and social circumstances (5).

There has been a significant change in how DSD is managed, especially over the past decade. There has also been a lot of activism around DSD and transsexual conditions. However, not much data has come out of Kenya. This audit aimed at establishing the current situation and act as a baseline for further research.

MATERIALS AND METHODS

Our main objective was to describe management of patients with DSD as practiced at Kenyatta National Hospital (KNH). We included all patients diagnosed with any disordered sexual development. Patients with missing files were excluded.

The study was a retrospective, longitudinal chart review, over a period of ten years (January 2003 to December 2013). Patient files at the KNH records department were retrieved using key words like disorders of sexual development, disorders of sexual differentiation, intersex, ambiguous genitalia, indeterminate sex, hermaphrodite and pseudohermaphrodite.

A data collection sheet was used in recording data. Data collected were then collated and analysed

using MS Excel spreadsheet. An approval by the University of Nairobi/KNH Ethics and Research Committee was sought before embarking on the study.

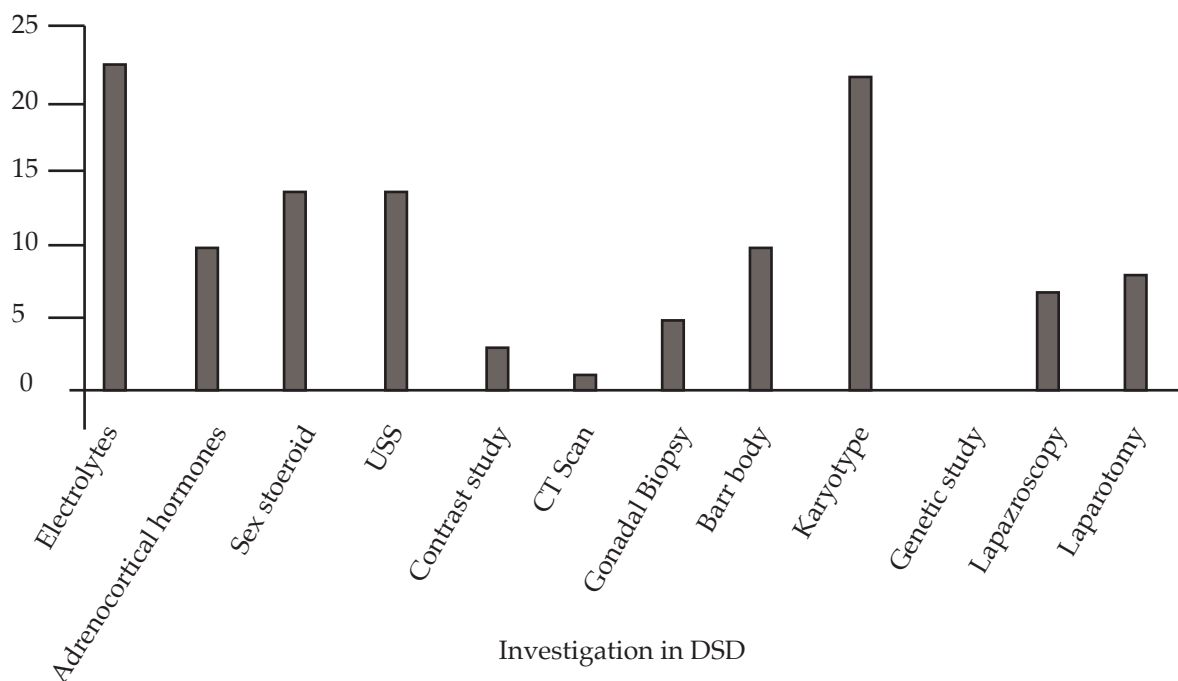
RESULTS

There were a total of 30 patients seen during the study period with retrievable records. It was not possible to know the number of missing files. Most of them (27, 92%) were born in a medical facility. Diagnosis was made by a medical person in all of them. The age at time of diagnosis was from birth to 19 years (median 5 months). Their calculated age during this review ranged from 1 to 29 years (median 8 years). Gender was assigned at birth in 28 (93%) patients. Fifteen patients were allocated male, 13 female and two had their gender allocation with held awaiting investigations. An initial diagnosis was stated as ambiguous genitalia/hermaphrodite in 26 (87%) of patients. There was an initial diagnosis of hypospadias and DSD in two cases each. One patient was lost to follow-up before being fully worked up.

The figure below depicts utilisation of investigative modalities in DSD at KNH:

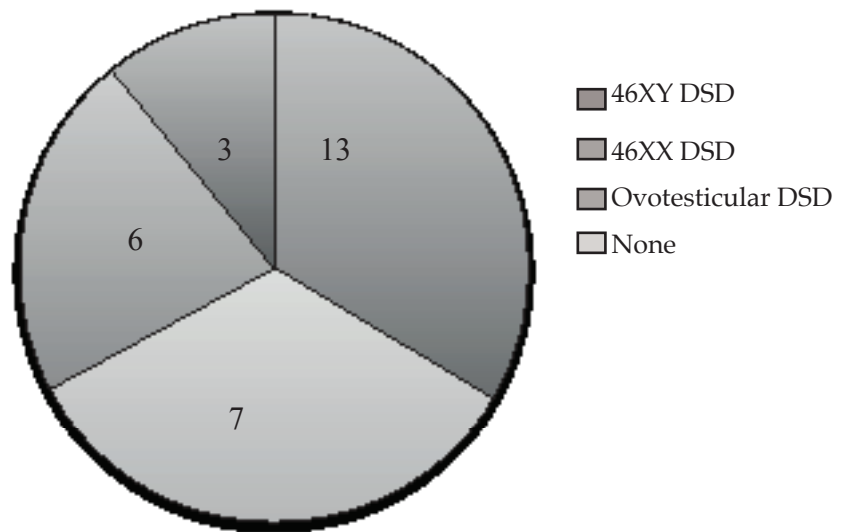
Figure 1

Diagnostic investigations done in patients with DSD at KNH



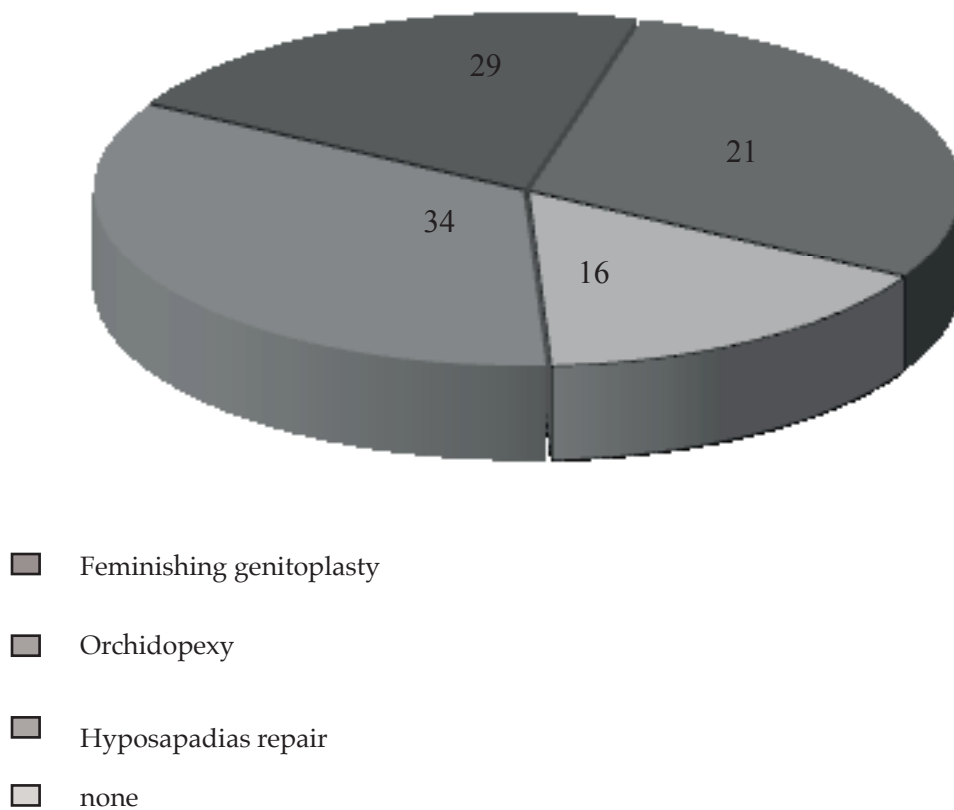
The figure below shows the final diagnosis arrived at after work up. One patient was lost to follow-up and six patients were still in the process of investigation at the time of data collection.

Figure 2
Final Diagnosis



Reconstructive surgery was carried out in 18 patients. There were 27 procedures carried out in total. Distribution of procedure groups was as shown in the figure below.

Figure 3
Surgical procedures



Gender reassignment was necessary in two patients, while three patients await the same. Among those who were re-assigned is a 14 year old who was brought up as boy with 46XX, DSD. She was reassigned to female gender at puberty and underwent feminising genitoplasty. Another patient was a four year old with 46XY, DSD who was brought up as a girl but after workup she was reallocated to the male gender. He then underwent hypospadias repair and orchidopexy.

All the three patients awaiting possible gender reassignment have 46XY, DSD, and have been brought

up as girls. Two of them have palpable gonads and all of them have perineal hypospadias. Presentation was uniformly late with pronounced male characteristics. The parents have chosen to stick with gender assigned at birth, and are still considering the way forward. There was no major psychological concern with the allocated gender. Amongst those whom the question was put, 11 (38%) were recorded to been satisfied, three (10%) were indifferent and 1 was not satisfied. 14 patients were not assessed for satisfaction with allocated gender.

Table 1
Classification of DSD

Previous	Revised
Female pseudohermaphrodite	46,XX DSD
Male pseudohermaphrodite	46,XY DSD
True hermaphrodite	Ovotesticular DSD
XX male	46,XX testicular DSD
XY sex reversal	46,XY complete gonadal dysgenesis

DISCUSSION

True incidence of DSD is usually difficult to estimate, but to be about 2.2 per 10,000 (2, 5). Incidence in Kenya is not known. Our figures show it's a relatively rare condition. Togo has an incidence of two cases per year, a similar number to our sample size of 30 (6, 22).

Data coming out of Africa is however insufficient (7). There is a big proportion of children who are born at home, and these patients, coupled with DSD being a source of stigma in many communities, present late (8). Despite this, most diagnoses are made within the first year of birth (median 5 months). There is tremendous pressure to allocate gender to all children immediately after birth, and this may lead to children being raised in genders that are not compatible with their physiology. There was however no patients or relatives who declined to follow medical advice, especially due to social pressures or cultural influence. Proper terminology has not fully picked up at KNH and this creates difficulties in managing the individual conditions that make up DSD spectrum. Previously, many diagnostic labels were used to describe DSDs. Current terminology is Disorders of Sexual Differentiation or Development (DSD), with an abbreviation of chromosomal makeup. This impacts on patient management, and avoids labels containing reference to gender (9). Precision when applying definitions and diagnostic labels is now a requirement.

Investigations done for DSD at KNH are not-uniform. This is attributable to the cost involved in most tests. Some tests like karyotyping and genetic studies are not available locally. No patient received

genetic tests to determine enzymatic defects. Most patients received multiple investigations and proper diagnosis was reached in 23 patients only.

Recommended investigations were done at KNH, but not all patients received similar investigations. For example, all patients should have had early estimation of electrolytes and adrenocortical hormones (76% and 33% respectively) to rule out salt losing enteropathy that can be life threatening. Ultrasound imaging is cheap and should have been universal, but only 14 patients had the procedure (15). Other investigations that should be done in all patients are laparoscopy, karyotype (Barr body test is not a substitute for karyotype, and its utility has diminished). Anatomical assessment should be done at birth or shortly thereafter, but it may also be necessary to do assessment in antenatal period and late childhood and adolescence (10-14).

The most common type of abnormality is 46 XX, DSD (60%), followed by 46 XY, DSD (20%). This was reflected in our study, with 46XX, DSD accounting for 43% and 46XY, DSD for 23%. A determination on etiology will be reached in most cases of 46XX DSD but only in about 50% of 46XY DSD (24). With a worldwide incidence of 1:15000, congenital adrenal hyperplasia, CAH, is the most common cause of DSD (2, 4).

Current recommendations is to withhold allocating a gender in a child born with indeterminate sex until investigations are concluded. This should be done as an emergency, and ideally the neonate should be kept in hospital for the whole duration. In Kenya, there is a dearth of laws that guide how DSD conditions are handled. At KNH, a multidisciplinary

team approach is employed early, and this is per the current recommended approach (2, 15, 20).

There has been significant changes in management of DSD. The current trend is to withhold any major reconstruction until much later when the patient can have a say (16,17). The paradigm is to do early diagnosis in the neonatal period, allocate a gender, but withhold any surgical procedures for later, especially those ones that drastically alter appearance (1, 3, 5, 18). Surgical care of DSD patients include:

- Virilised female: Feminising genitoplasty and including vaginoplasty and clitoroplasty. 16% of our patients had these procedures
- Undervirilised males: Hypospadias repair and reconstruction. Orchidopexy, scrotorraphy and phalloplasty are other procedures carried out. 55% of our patients had these procedures.
- Gender reassignment may be considered in some patients with genital inadequacy (19). Only two patients received gender reassignment procedures.

In our patients, there was delayed gender reallocation and reconstructive surgery. Oludayo *et al* evaluated DSD patients admitted at a Nigerian hospital over 14 year period. He evaluated all cases treated (n=9). It was necessary to change sex of rearing in 2 cases (23). This is similar to what we found.

These practices at KNH are similar to the recommendations made by the working party on DSD held at Annecy France in 2012 where they recommended avoiding gender assignment before complete evaluation of an infant with suspected DSD (11, 12, 21).

In conclusion, this study has shown a lack of uniformity in management of DSDs at KNH. Generally, however, management was acceptable.

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