DOI: https://doi.org/10.53350/pjmhs22166116

ORIGINAL ARTICLE

Karyotypic Analysis of Children with Disorders of Sex Development (DSD) at Children Hospital & ICH, Lahore

SARAH KHAN[1], AREIBA HAIDER[2], RAAFEA TAFWEEZ[3]
[1,2]Assistant Professor of Anatomy, King Edward Medical University, Lahore
[3]Professor of Anatomy, King Edward Medical University, Lahore
Correspondence to Dr. Sarah Khan, Assistant Professor Anatomy, Email: sarahkhan104@hotmail.com

ABSTRACT

Aim: To determine the frequency of different karyotypes in children with DSD presented at The Children Hospital & ICH, Lahore
Study design: Cross sectional analytical
Place and Duration of Study: Department of Genetics, Children Hospital and ICH, Lahore, from Jan 2016 to June 2017.
Methodology: The study was conducted on 83 adolescent children with any form of DSD after taking an informed consent. A detailed history was taken and sex of rearing was noted. Physical examination was done to know the morphological sex while karyotyping of all the cases was done for the confirmation of their genetic sex. All the findings were recorded on a predesigned proforma. The cases that have undergone any surgical correction procedure for genital ambiguity were excluded. Data was analyzed by SPSS 21.
Results: Out of 83 cases, 27(32.5%) cases were reared as male at birth while 56(67.4%) were reared as female. Karyotypic analysis was done in all 83 cases. 27 cases who were reared as male, their karyotypic analysis of male sex of rearing showed a chromosomal compliment of 46XY in 25(92.5%), 46XX in 01(3.7%), 46XXY in 01(3.7%). Out of 56 cases of female sex of rearing, 45(80.3%) had 46XX karyotype 03(5.3%) had 46XY karyotype, 45X0 in 07(12.5%) and one case (1.7%) showed a XXX karyotype.
Conclusion: To ensure the high-quality life for such an individual, there is an urgent need for correct sex assignment. Chromosomal analysis is important as a first step in determining an accurate genetic sex before the costly diagnostic tests and surgical procedure.
Keywords: Intersex, Ambiguous genitalia, Karyotyping

INTRODUCTION

Disorders of sex development (DSD) are the congenital conditions in which the development of chromosomal, gonadal or anatomical sex is atypical. In 2006, Lawson Wilkins Paediatric Endocrine Society (LWPES) and European Society for Paediatric Endocrinology (ESPE) classified these disorders as 46XX DSD, 46XY DSD and sex chromosome DSD. 46XX DSD are females having male looking external genitalia and 46XX karyotype. 46XY DSD are males with female phenotype and 46XY chromosomal compliment. Sex chromosomal DSD consists of Turner's syndrome and Klinefelter's Syndrome with their variants[1].

Ambiguous genitalia is the most common presentation in cases of DSD with a worldwide prevalence of about 1:4500.[2] In the United States one in 2000 children, or five children per day, are born with sexual ambiguity[3]. In Germany 2.2/10,000 cases were reported with ambiguous genitalia at birth[4].

The incidence of intersex due to congenital adrenal hyperplasia is found to be 1 per 15000 live births in great Britain.[5] An accurate sex assignment at birth gives the child a healthy psychological development and confidence[6].

The objective of the study was to determine the frequency of different karyotypes in children with DSD presented at The Children Hospital & ICH, Lahore

METHODOLOGY

The study was conducted on 83 Children with various forms DSD at The Children Hospital & ICH, Lahore from May 2016 to May 2017 after taking ethical approval from the Institutional Review Board of the hospital. All the Children above10 years of age with any type of DSD were included in the study after taking an informed consent from their parents or guardians. Cases that have already undergone any surgical correction procedure for genital ambiguity, delayed puberty due to systemic diseases were excluded. A detailed history was taken regarding parameters such as sex of rearing, amenorrhea, hirsutism, gynecomastia, delayed puberty, cyclic hematuria etc. External genital examination was carried out in a separate room and in the presence of either parent by maintaining complete privacy and confidentiality. All the cases underwent karyotypic analysis for the determination of their genetic sex. For karyotyping 2ml blood sample of the patient was collected in the Lithium-Heparin vial. Mononuclear cells were purified and cultured in a nutrient-enriched medium for a period of 72 hours. At the end of culture, it was treated with colcemid to arrest the cells in metaphase of mitosis. Afterwards slide preparation and staining was done with GIEMSA stain. Data collected was entered and analyzed by using SPSS 21 version.

Received on 12-11-2021
Accepted on 23-05-2022

RESULTS

A total of 83 cases of DSD were studied. The mean age at presentation was 14.5±1.5 years. 27(32.5%) were reared as male at birth while 56(67.4%) were reared as female by their parents.

Fig. 1: Karyogram showing a karyotype of Turner's syndrome (45X0)

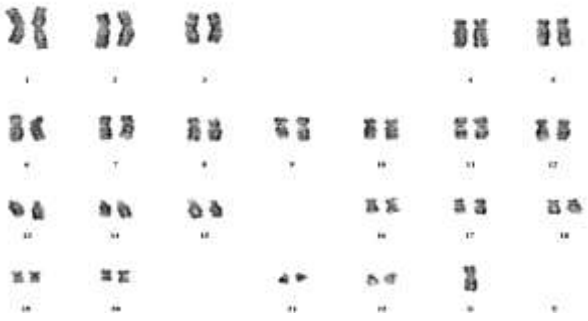

Table 1: Presenting complaints in DSD

Presenting Complaints	Male (n=27)	Female (n=56)
Primary amenorrhea	0(0%)	35(62%)
Cyclic hematuria	0(0%)	0(0%)
Delayed puberty	08(30%)	14(25%)
Gynaecomastia	01(4%)	0(0%)
Hirsutism	0(0%)	02(4%)
Genital ambiguity	18(66%)	05(9%)

Table 2- Karyotypic Analysis in DSD

Karyotypic Sex	**Male**	**Female**
46XY	25(92.5%)	03(5.3%)
46XX	01(3.3&%)	4580.3%)
Turner syndrome (45X0)	00	0712.5%)
Klinefelter syndrome (47XXY)	013.7%)	00
XXX female	00	1(1.7%)
Total	27(100%)	56(100%)

Fig. 2: Karyogram showing a karyotype of Klinefelter's Syndrome (47XXY)

DISCUSSION

In this study, the mean age at presentation was14.5±1.5 years. These children did not get any treatment of DSD at an early age.The reporting age of DSD in other developing countries is also late adolescence or early adulthood.[7] Similar data of age at presentation was recorded from Turkey and India.[8] The logical reason for this late presentation could be lack of awareness, socioeconomic issues and cultural taboos. In Pakistan, the parents feel hesitation in seeking any medical advice at an early age until some other signs of intersexuality develop with the development of secondary sexual characteristics and affect the social life of their children. On the other hand, in developed countries where DSD is not considered as a taboo because of public awareness, the age at presentation is at birth or early childhood.[9] Thailand has started the multidisciplinary management of ambiguous genitalia very early in 1979[10].

Klinefelter's syndrome is a consequence of an extra X-chromosome in males (46XXY) and its diagnosis is rarely made before puberty because of paucity of clinical manifestations and normal male external genitalia at birth.[11] Turner's syndrome appears as a result of one missing X chromosome in females (45X0) and is diagnosed in late childhood or adolescence during investigation of short stature or delayed puberty[12]. Higher frequency of Turner's syndrome as compared to Klinefelter's syndrome was seen in our study similar to studies in Turkey[15] and Pakistan[13].

CONCLUSION

The present study showed the importance of early karyotypic analysis as an initial step in the management of disorders of sex development. Late diagnosis leads to social maladjustment, psychological issues and wastage of useful human resources.

Conflict of interest: Nil

REFERENCES

1. Pasterski V, Prentice P, Hughes IA. Consequences of the Chicago consensus on disorders of sex development (DSD): current practices in Europe. Arch Dis Child. 2010;95(8):618-23
2. Monlleo IL, Zanotti SV, Araujo BP et al. Prevalence of genital abnormalities in neonates. J Pediatr (Rio J). 2012;88(6):489-95.
3. How common is intersex? Intersex Society of North America. Isna.org. available from http://www.isna.org/faq/frequency.
4. Anke L, Siegfried K, Eva K et al. Clinical evaluation study of the German network of disorders of sex development (DSD)/intersexuality: study design, description of the study population, and data quality. *BMC Public Health.* 2009 Apr 21; 9:110.
5. Khalid JM, Oerton JM, Dezateux C et al. Incidence and clinical features of congenital adrenal hyperplasia in Great Britain.*Arch Dis Child.* 2012 Feb; 97(2):101-6.
6. Cohen-Kettenis PT. Psychosocial and psychosexual aspects of disorders of sex development. *Best Pract Res Clin Endocrinol Metab.* 2010;24:325–34.
7. Manzoor J, Aftab S, Yaqoob M. Ambiguous genitalia: An overview of 7 years experience at the Children's Hospital & Institute of Child Health, Lahore, Pakistan. Pak J Med Sci. 2019 Jan-Feb; 35(1): 151–155.doi: 10.12669/pjms.35.1.289
8. Erdogan S, Kara C, Ucakturk A et al. Etiological Classification and Clinical Assessment of Children and Adolescents with Disorders of Sex Development. J Clin Res Pediatr Endocrinol. 2011;3(2):77–83
9. Ozbey H, Etker S. Disorders of sexual development in a cultural context. Arab J Urol. 2013;11(1):33-39
10. Nimkarn S, Sangacharoenkit P, Sawathiparnich P et al. Ambiguous genitalia: an overview of 22 years experience and the diagnostic approach in the Pediatric Department, Siriraj Hospital. *Journal of the Medical Association of Thailand*. 2002; 85 (2):496-505.
11. Bojesan A, Juul S, Gravholt CH. Prenatal and postnatal prevalence of Klinefelter syndrome: a national registry study. *J Clin Endocrinol Metab.* 2003; 88:622-26.
12. C H. Epidemiological, endocrine and metabolic features in Turner syndrome. *Eur J Endocrinol.* 2004; 151:657-87.
13. Rehman UL, Ahsan T, Jabeen R et al. Clinical Spectrum of Disorders of Sexual Differentiation. J Coll Physicians Surg Pak. 2016;26(3):199-203