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ORIGINAL ARTICLE

Profile of patients with genitourinary anomalies treated in a clinical genetics service in the Brazilian unified health system

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KEYWORDS
Genitalia;
Sexual differentiation/genetics;
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Abstract
Objective: To describe the profile of patients with genitourinary abnormalities treated at a tertiary hospital genetics service.
Methods: Cross-sectional study of 1068 medical records of patients treated between April/2008 and August/2014. A total of 115 cases suggestive of genitourinary anomalies were selected, regardless of age. A standardized clinical protocol was used, as well as karyotype, hormone levels and genitourinary ultrasound for basic evaluation. Laparoscopy, gonadal biopsy and molecular studies were performed in specific cases. Patients with genitourinary malformations were classified as genitourinary anomalies (GUA), whereas the others, as Disorders of Sex Differentiation (DSD). Chi-square, Fisher and Kruskal–Wallis tests were used for statistical analysis and comparison between groups.
Results: 80 subjects met the inclusion criteria, 91% with DSD and 9% with isolated/syndromic GUA. The age was younger in the GUA group ($p<0.02$), but these groups did not differ regarding external and internal genitalia, as well as karyotype. Karyotype 46,XY was verified in 55% and chromosomal aberrations in 17.5% of cases. Ambiguous genitalia occurred in 45%, predominantly in 46,XX patients ($p<0.006$). Disorders of Gonadal Differentiation accounted for 25% and congenital adrenal hyperplasia, for 17.5% of the sample. Consanguinity occurred in 16%, recurrence in 12%, lack of birth certificate in 20% and interrupted follow-up in 31% of cases.

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Conclusions: Patients with DSD predominated. Ambiguous genitalia and abnormal sexual differentiation were more frequent among infants and prepubertal individuals. Congenital adrenal hyperplasia was the most prevalent nosology. Younger patients were more common in the GUA group. Abandonment and lower frequency of birth certificate occurred in patients with ambiguous or malformed genitalia. These characteristics corroborate the literature and show the biopsychosocial impact of genitourinary anomalies.

PALAVRAS-CHAVE
Genitália;
Diferenciação sexual/genética;
Etiologia

Perfil de pacientes com anormalidades geniturinárias atendidos em serviço de genética clínica no sistema único de saúde

Resumo
Objetivo: Descrever o perfil de pacientes com anormalidades geniturinárias atendidos em serviço de genética de hospital terciário.
Métodos: Estudo transversal de 1.068 prontuários de pacientes atendidos entre abril/2008 e agosto/2014. Foram selecionados 115 casos sugestivos de anomalias geniturinárias, independentemente da idade. Usaram-se protocolo clínico padronizado, cariótipo, hormônios e ultrassonografia geniturinária para avaliação básica. Laparoscopia, biopsia gonadal e estudos moleculares foram feitos em casos específicos. Pacientes com malformações geniturinárias foram classificados como defeitos geniturinários (DGU), os demais, como distúrbios da diferenciação do sexo (DDS). Usaram-se qui-quadrado, Fisher e Kruskal-Wallis para análise estatística e comparação entre os grupos.
Resultados: Preencheram os critérios de inclusão 80 sujeitos, 91% com DDS e 9% com DGU isolados/sindrômicos. A idade foi menor no grupo DGU ($p<0,02$), mas esses grupos não diferiram quanto a genitália externa, interna e cariótipo. Verificou-se cariótipo 46,XY em 55% e aberrações cromossômicas em 17,5% dos casos. Ambiguidade genital ocorreu em 45%, predominou em pacientes 46,XX ($p<0,006$). Distúrbios da diferenciação gonadal representaram 25% e hiperplasia adrenal congênita; 17,5% da amostra. Consanguinidade ocorreu em 16%, recorrência em 12%, ausência de registro civil em 20% e interrupção do seguimento em 31% dos casos.
Conclusões: Predominaram pacientes com DDS. Ambiguidade genital e diferenciação sexual anômala foram mais frequentes entre recém-nascidos e pré-púberes. Hiperplasia adrenal congênita foi a nosologia mais prevalente. Pacientes mais jovens pertenciam ao grupo DGU. Menor frequência de registro civil e abandono ocorreram em pacientes com genitália ambígua ou malformada. Essas características corroboram a literatura e evidenciam o impacto biopsicossocial das anormalidades geniturinárias.

Introduction

Genitourinary abnormalities (GUA) represent 35–45% of birth defects and include a wide range of structural abnormalities of the urinary and reproductive tracts, whose collective occurrence reflects their embryological origin and common genetic control.[1–3] The clinical spectrum extends from minor anomalies such as glandular hypospadias to severe conditions such as bladder exstrophy. The clinical presentation may be isolated or associated with other anatomical defects and present syndromic conditions. The etiology comprises genetic causes resulting from chromosomal, monogenic or multifactorial abnormalities, not genetic, associated with exposure to teratogens, and there also the unknown causes.[1,4]

Disorders of Sex Differentiation (DSD) are a special group of GUA in which the development of genetic, gonadal or anatomical sex is atypical or incongruous. Clinical manifestations range from classical genital ambiguity, manifested at birth, to infertility in adults.[4,6–11] Clinical heterogeneity and the use of different inclusion criteria, collecting methods, coding and recording of GUA account for wide variations in prevalence. With the exception of minor abnormalities, such as isolated hypospadias with a prevalence of 1:250 live births, some disorders may be as rare as 1:100,000, as in cloacal exstrophy.[12,13] In the SDD group, a global prevalence of 1–2:10,000 births is assumed,[2,4,9,11] which put these conditions in the group of so-called rare diseases, recent focus of health care policies in genetics in the National Health System (Sistema Único de Saúde – SUS).[14]

The management of patients with GUA requires a multidisciplinary approach in view of the underlying complex surgical, endocrine, genetic, social, psychological, and ethical issues.[4,6–10] All these aspects make GUA an important