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How often are clinicians performing genital exams in children with disorders of sex development?

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Abstract

Background: We sought to determine the frequency with which genital exams (GEs) are performed in children with disorders of sex development (DSD) and ambiguous genitalia (AG) during routine visits to the pediatric endocrine clinic.
Methods: Medical records of children with DSD and AG seen at one large academic center since 2007 were reviewed. Data analyzed included diagnosis, sex of rearing, age, initial or follow up visit, number of individuals present and sex of the pediatric endocrinologist. Repeated measures analysis was performed to evaluate associations between GEs and patient/physician factors.
Results: Eighty-two children with DSD and AG who had a total of 632 visits were identified. Sex of rearing was female in 78% and the most common diagnosis was congenital adrenal hyperplasia (CAH) (68%). GEs were performed in 35.6% of visits. GEs were more likely in patients with male sex of rearing (odds ratio [OR] 17.81, $p = 0.006$), during initial vs. follow-up visits (OR 5.99, $p = 0.012$), and when the examining endocrinologist was female (OR 3.71, $p = 0.014$). As patients aged, GEs were less likely (OR 0.76, $p < 0.0001$).
Conclusions: GEs were performed in approximately one-third of clinic visits in children with DSD and AG. Male sex of rearing, initial visits and female pediatric endocrinologist were associated with more frequent GEs.

Keywords: ambiguous genitalia (AG); clinical decision making; clinical management of disorders of sex differentiation; congenital adrenal hyperplasia; disorders of sex development (DSD).

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Introduction

Disorders of sex development (DSD) are rare congenital conditions in which development of gonads, chromosomes, or anatomic sex is atypical. Many DSD are associated with ambiguous genitalia (AG) and are typically diagnosed at birth [1–3]. Over the past 15 years, the care of children with DSD and AG has evolved into a more nuanced approach to sex assignment, an emphasis on multi-disciplinary care, and a recognition of the importance of minimizing psychosocial stressors for patients and families [4, 5]. Adults with DSD have verbalized that being subjected to frequent genital exams (GEs) by multiple providers throughout childhood is a significant source of stress. Thus, current guidelines recommend limiting GEs in the outpatient setting [4, 6], although an optimal number of such exams has not been specified. However, the extent to which pediatric endocrinologists actually perform routine GEs in children with DSD and AG has not been examined. We sought to determine how often GEs are performed in children with DSD and AG in the pediatric endocrine clinic and whether there are patient and/or physician characteristics associated with a greater likelihood of performing an exam. We hypothesized that GEs are less likely in patients beyond toddler age, and when more people are present in the exam room. In addition to age, we speculated that there may also be differences in the frequency of GEs based on the patient's diagnosis, sex of rearing and type of visit, as well as the sex of the physician. We were particularly interested in clinical practice since publication of the 2006 statement from the international consensus conference on the management of intersex disorders [4].

Patients and methods

A retrospective review of medical records of children followed in the Riley Pediatric Endocrine Clinic for DSD between January 1, 2007 and September 30, 2014 was performed. The Institutional Review Board approved the study for exemption due to the retrospective nature and de-identified data collection. Using ICD-9 codes and diagnoses within physician notes, we searched for congenital adrenal hyperplasia (CAH), mixed gonadal dysgenesis, partial androgen

insensitivity syndrome, cloacal exstrophy, and AG not otherwise specified. Patients with only one clinic visit were excluded from the analysis.

Data were extracted through review of physician dictations for each clinic visit within the study period. Variables collected and analyzed included patient age, patient sex of rearing, diagnosis, type of clinic visit (new versus follow up), sex of pediatric endocrinologist, number of people in the exam room, and whether a GE had been performed. Due to the low frequency of some diagnoses (partial androgen insensitivity syndrome, cloacal exstrophy), diagnostic categories were created to perform the multivariate regression. Diagnostic categories included CAH, mixed gonadal dysgenesis (GD), and AG not otherwise specified. A GE was considered to have taken place when notes described clitoromegaly/phallus/penis, scrotum/labia, genital mucosa, urogenital sinus, or testicular palpation. GE was considered to not have been performed when dictations included a statement of deferred GE, no information pertaining to GE, or only a comment on pubic hair Tanner stage.

Data were stored in Microsoft Excel and analyzed using SAS (Version 9.4). The level of significance for all tests was $\alpha = 0.05$. Basic descriptive statistics were calculated to characterize the study population, including frequencies, percentages, means and standard deviations. The relationship between of the frequency of GEs and year of examination was assessed using Pearson's correlation. Repeated measures analysis and multiple logistic regression were used to assess the relationship between GEs and patient or physician characteristics. The primary outcome variable was whether a GE had been performed.

Results

Ninety-seven patients were identified, of whom 82 were seen at least twice, comprising a total of 632 clinic visits. The average age was 9.6 years, and ranged from 1 week to 22 years. Most visits (60%) were for children less than age 12 years. Sex of rearing was female in 64 (78%) and male in 18 (22%). The most common diagnosis was CAH, comprising 80.1% of all visits. The average number of clinic visits per patient was 8. The pediatric endocrinologist was female in 417 of the visits (65.9%). Across all visits, GEs were performed in 225 (35.6%). Patient characteristics are summarized in Table 1.

On repeated measures multivariate regression analysis, patients with a male sex of rearing were found to have 17.81 higher odds of having a GE performed ($p = 0.006$), whereas patients with a female sex of rearing were less likely to have a GE performed (odds ratio [OR] 0.32, $p = 0.021$).

The type of visit was also associated with a higher likelihood of a GE being performed, with new patient visits having an OR of 5.99 ($p = 0.012$) compared to follow up visits. Female pediatric endocrinologists were more likely to include a GE compared to male colleagues, with an OR of 3.71 ($p = 0.014$, 95% CI: 1.31–10.53). Specifically, GEs were performed in 41% of all clinic visits in which the pediatric endocrinologist was female compared with 25% of visits in which the examining physician was male. Of the 225 visits in which GEs were performed, the pediatric endocrinologist was female in 76% ($n = 171$).

Table 1: Study population characteristics and descriptive statistics.

Patient characteristics	
Study population, n	82
Age, years (mean, SD)	9.6 (5.9)
Female sex of rearing, n (%)	64 (78%)
Total number of visits, n	632
Visits with female endocrinologists, n (%)	417 (66%)
Visits with male endocrinologists, n (%)	215 (34%)
Diagnosis, n (%)	
Congenital adrenal hyperplasia	56 (68.3%)
Mixed gonadal dysgenesis	7 (8.5%)
Partial androgen insensitivity syndrome	1 (1.2%)
Cloacal exstrophy	1 (1.2%)
Ambiguous genitalia, NOS	17 (20.7%)
Visits in which GE was performed, n	225
GE's performed by female endocrinologists, n (%)	171 (76%)
GE's performed by male endocrinologists, n (%)	54 (24%)

In contrast, no statistically significant association was observed between the performance of GEs and patient diagnosis (CAH: $p = 0.084$, MGD: $p = 0.223$, AG: $p = 0.648$). Similarly, the year of the visit ($p = 0.447$) and the number of people documented to be present during the visit ($p = 0.623$) were not significantly associated with whether a GE had been performed. These results are summarized in Table 2 and Figure 1.

Additional analyses revealed that patients were significantly less likely to undergo GEs as they aged. The odds of a GE being performed declined by 0.76 for every year a patient aged ($p < 0.001$). Although the rate of GE performance varied by year, no linear association between years

Table 2: Summary of repeated measures multivariate logistic regression results.

Variable	Odds ratio	95% CI
Results of repeated measures analysis		
Diagnosis		
CAH	3.74	0.84–16.69
MGD	2.6	0.56–12.07
AG	1.42	0.32–6.31
Male sex of rearing	17.81	2.28–139.06
Female sex of rearing	0.32	0.12–0.85
Age	0.76	0.70–0.81
Initial visit	5.99	1.48–24.19
Year of visit	0.94	0.81–1.10
Number of people present in exam room	1.07	0.82–1.41
Female pediatric endocrinologist	3.71	1.31–10.53

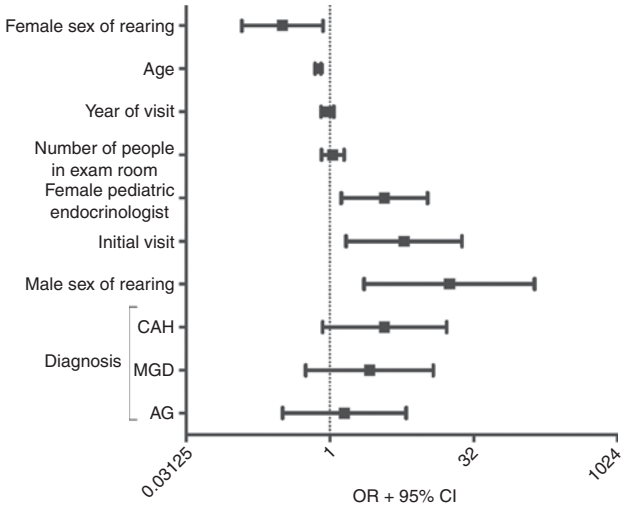

Figure 1: Multivariate logistic regression results showing odds ratios and confidence intervals (along x-axis) of modeled predictor variables (along y-axis).
Outcome variable was performance of GE.

following DSD guidelines and the frequency of GEs was observed (Pearson's r = −0.124, p = 0.778).

Discussion

DSD are conditions that present considerable challenges for patients, their families, and providers. Children with DSD experience substantial psychosocial stress, reporting significantly lower measures of self-esteem and physical well-being in studies of health-related quality of life compared with the general population [1]. For adults with DSD and AG, overall satisfaction with medical care is significantly lower than for adults with other chronic conditions (http://www.dsdguidelines.org/files/clinical.pdf). Parents and caregivers of children with DSD are also affected and have been described to have significant rates of depression, anxiety and symptoms of post-traumatic stress [1, 7–10].

It has long been recognized that frequent GEs are unnecessary, intrusive and a major contributor to psychological distress among individuals with DSD and AG [2, 4, 6, 7, 10, 11]. While greatly limiting such exams has been generally acknowledged to be a goal, the degree to which GEs are being deferred in the outpatient setting has not been quantified nor has a specific limitation to the number of exams been specified. To our knowledge, ours is the first study to assess the frequency with which pediatric endocrinologists performed GEs at one large pediatric endocrine practice in the years following published guidelines that included recommendations to restrict such exams.

The much higher rate of GEs among patients with a male sex of rearing can likely be attributed to many of these children having at least one palpable gonad. Physician dictations included details on gonadal consistency and size likely driven by concerns about an increased risk of gonadal neoplasia in the setting of a DSD. Notably, many of these same patients also underwent surveillance in the form of testicular ultrasounds, again due to concerns about gonadal malignancy [12].

Patient age was significantly inversely related to the likelihood that a GE was performed, which seems intuitive and is in accordance with current DSD and AG recommendations [4–6], although a precise age at which these exams should be limited has not been specified. Clinicians also tended to perform GEs on initial rather than follow up visits, likewise demonstrating adherence with the goal of limiting the frequency of such exams. For many of the patients in this cohort, GEs were performed in follow up visits only if the patient had recently undergone genital surgery or if guardians presented concerns of suspected anatomic changes. With these exceptions, explicit documentation of clinical indication or medical reasoning for the performance of a GE was absent in the majority of the visits reviewed.

Intriguingly, our findings also suggest that female physicians may be more likely to do GEs than male physicians although the small number of males in our sample (n = 4) may have skewed this result. If corroborated, whether this reflects a gender differential in comfort level with such exams or some other dimorphic phenomenon is unclear.

Limitations of our study include the small sample size of some diagnostic categories and the fact that it was retrospective. It is always possible that a GE was performed but was not documented in the medical record. How generalizable our findings are is also of question. However, as a group of 12 pediatric endocrinologists at a large tertiary care center, we suspect that our practice is fairly reflective of what occurs at other academic institutions. Lastly, an "ideal" frequency of GEs in this clinical population has not been defined, rendering it impossible to evaluate our findings in comparison to a gold standard of clinical care. Since data on the frequency of GEs prior to publication of the 2006 consensus guidelines are lacking, we are unable to comment on whether the degree to which they are performed has changed over time.

Conclusions

To our knowledge, this is the first study to quantify the frequency of GEs in children with DSD and AG in the

outpatient setting at one large academic center following consensus guidelines. We believe that it is reassuring that GEs were performed in only approximately one-third of clinic visits. Whether eliminating frequent GEs will have a significant impact on psychosexual and social outcomes in patients with DSD and their families' remains to be seen. Large-scale prospective studies investigating specific aspects of management in children with DSD and AG are needed to inform the development of guidelines delineating indications for and recommended frequency of GEs in this clinical population.

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