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Genetic testing of DSD patients in Ukraine

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Background

In this study we investigated the genetic aetiology of a series patients with DSD seen in Ukraine

Methods

In 2018y the Ukraine Pediatric DSD Register included 95 children with DSD between the ages of 0-18 y.o. (a prevalence of 1 in 80097). The criterion for including patients to the database was ambiguous genitalia and/or a discrepancy between the chromosomal and gonadal/genital sex. All patients had a karyotype performed and, if necessary, fluorescence in situ hybridization (FISH).
We studied 30 probands with 46,XX or XY DSD for further exome sequencing studies.

Results

Figure 1. Structure of DSD in Ukraine

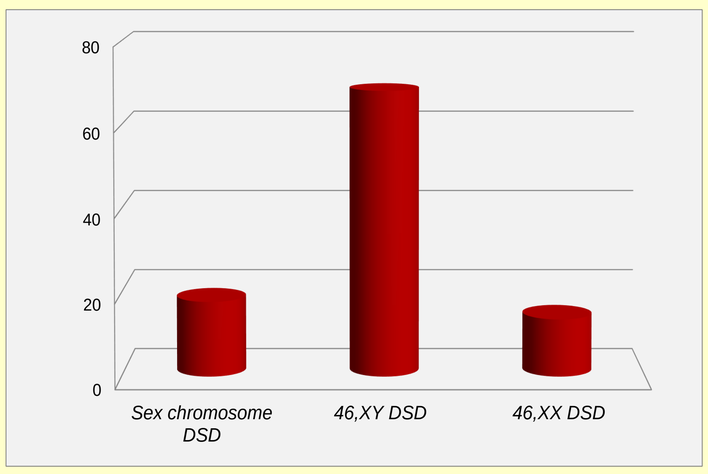


Figure 2. 46,XY DSD, n=65 (m/f ratio, %)

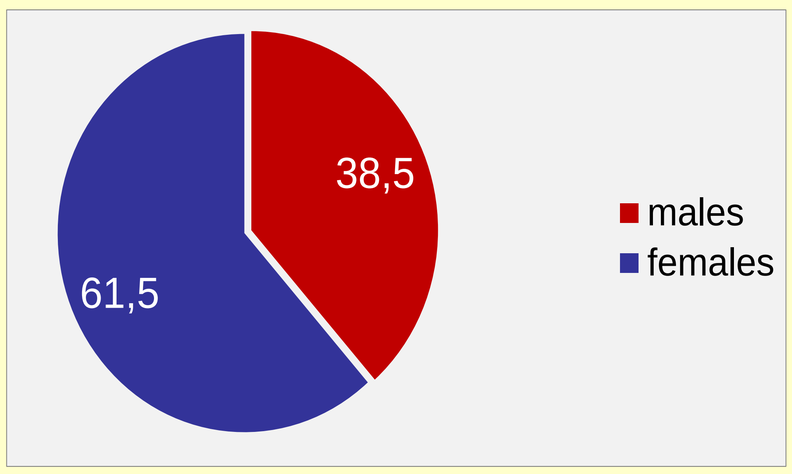
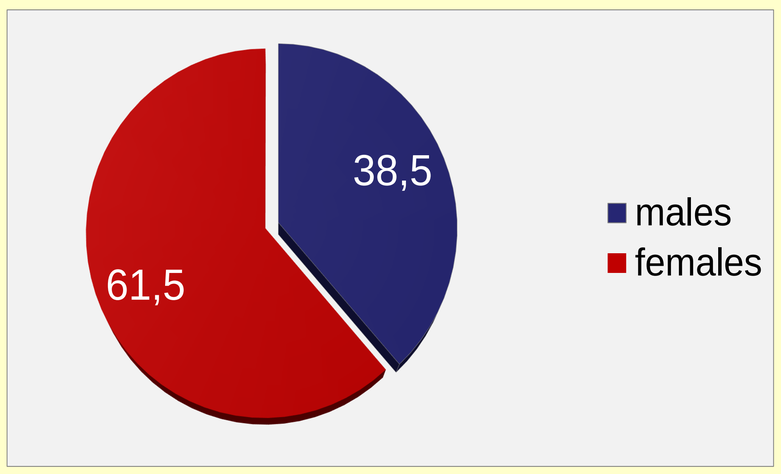


Figure 3. 46,XX DSD, n=13 (m/f ratio, %)



The most frequent variant of the karyotype among the first group was 45,X/46,XY (n=6; 35.2%).
In a group of patients with 46,XX DSD we diagnosed: testicular 46,XX DSD (n=5), 21-hydroxylase deficiency with virilization IV-V degree by Prader (n=4), 46,XX gonadal dysgenesis (n=3) and DSD in VACTER-association (n=1).

Figure 4. **Genetic cause of DSD (n=18)**

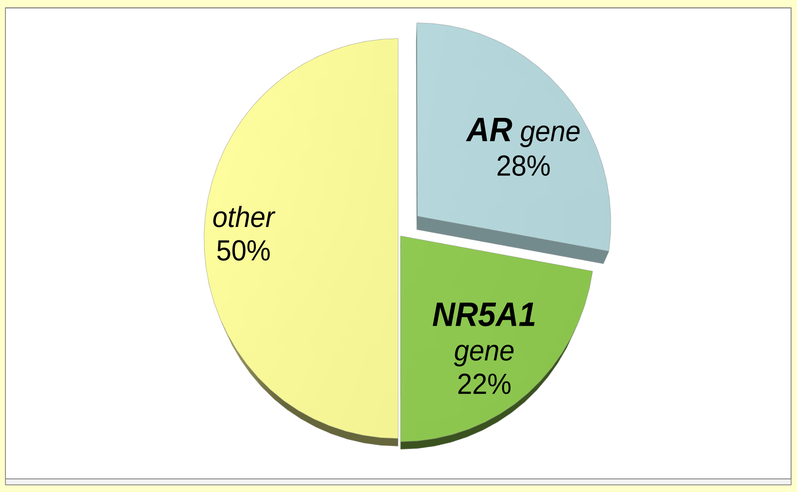


Table 1. **Other genetic findings in 46,XY DSD (n=9, 50%)**

MYRF	2
WT1	1
DHX37	1
CBX2	1
SRD5A2	1
HSD17B3	1
AMHR2	1
KAL	1

Genetic testing in 46,XY/XX DSD group was done in 30 (38.4%) cases.
We determined the genetic etiology in 18 of 30 (60%) probands diagnosed with DSD. We report that *AR (n=5)* and *NR5A1 (n=4)* mutations are the commonest cause of 46,XY DSD in Ukraine, accounting for 50% of cases. Other genetic causes of 46, XY DSD included *MYRF (n=2), WT1, SRD5A2, HSD17B3, DHX37, AMHR2, KAL* and *CBX2* variants.
In 7 patients (23.3%) we found VUS variants and their causality should be proven in further studies.
A multi-disciplinary team has been created for gender assignment in DSD newborns and to improve the decisions of further clinical management, including the time of gonadectomy.

Conclusions

Genomic analysis found a genetic cause in the majority of cases. Further studies to identify novel genes causing DSD are required.