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

Methods

In 2018, 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

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 VACTERL association (n=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.