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Novel associations in disorders of sex development: findings from the I-DSD Registry

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Context: The focus of care in disorders of sex development (DSD) is often directed on issues related to sex and gender development. In addition, the molecular etiology remains unclear in the majority of cases.

Objective: To report the range of associated conditions identified in the I-DSD Registry.

Design, Setting & Patients: Anonymized data were extracted from the I-DSD Registry for diagnosis, karyotype, sex of rearing, genetic investigations and associated anomalies. If necessary, clarification was sought from the reporting clinician.

Results: Of 649 accessible cases, associated conditions occurred in 168 (26%); 103 (61%) cases had one condition, 31 (18%) two, 20 (12%) three and 14 (8%) four or more. Karyotypes with most frequently reported associations included 45,X with 6/8 affected cases (75%), 45,X/46,XY with 19/42 cases (45%), 46,XY with 112/460 cases (24%) and 46,XX with 27/121 cases (22%). In the 112 cases of 46,XY DSD, commonest conditions included small for gestational age (SGA) in 26 (23%), cardiac anomalies in 22 (20%) and CNS disorders in 22 (20%), while in the 27 cases of 46,XX DSD, skeletal and renal anomalies were commonest at 12 (44%) and 8 (30%), respectively. Of 170 cases of suspected Androgen Insensitivity Syndrome (AIS), 19 (11%) had reported anomalies and 9 of these 19 had confirmed androgen receptor mutations.

Conclusions: Over a quarter of cases in the I-DSD Registry have an additional condition. These associations can direct investigators towards novel genetic etiology and also highlight the need for more holistic care of the affected person.