Erhebungseinheit für seltene pädiatrische Erkrankungen in Deutschland

Forschungsstelle für pädiatrische Epidemiologie der Deutschen Gesellschaft für Kinder- und Jugendmedizin e.V.

UNIVERSITÄTSmedizin. MAINZ

Newborns and children with an inital diagnosis of intersex/variation of sexual development or 46,XX congenital adrenal hypoplasia (CAH) with virilised genitalia

Objectives:
The primary aim of the study is to determine the prevalence of children with DSD (Differences of Sexual Development) at birth and during the first 28 days of life. Secondary study objectives are the recording of the phenotype, karyotype, molecular genetic examinations, recommendations of the centres/specialists for further care/counselling

Management:
Prof. Dr. Annette Richter-Unruh (Kontaktperson), Universitätsklinikum Ulm, Klinik für Kinder- und Jugendmedizin, Sektion Pädiatrische Endokrinologie und Diabetologie, Eythstraße 24, 89075 Ulm, aru@labmed.de
Prof. Dr. Clemens Kamrath, Universitätskinderklinik Freiburg, clemens.kamrath@uniklinik-freiburg.de
Dr. Uta Neumann, Charité Berlin, uta.neumann@charite.de

Duration oft he study: 3 years, start: 07/2023

Background:
The options for surgical treatment of children who are unable to give consent are significantly restricted by the 2021 Act on "Protection of Children from Gender Reassignment Surgery" [1] and are only possible in special cases, such as urogenital sinus or penile shaft straightening, following authorisation by the family court. Surgical treatment of the genitals is generally not indicated in the neonatal period. To date, studies on surgical interventions in newborns and children are limited, and studies on the long-term prognosis in particular are insufficient. However, almost all 46,XX-CAH (congenital adrenal hypoplasia) girls have undergone surgery in infancy and genital reassignment surgery has been performed regularly. Concrete numbers are not available due to a lack of data or registry. Currently, an unexpectedly large number of infants, especially those with severe hypospadias, are being presented to the interdisciplinary commission for a statement in the study centres involved in the study (Ulm, Freiburg, Berlin).

Questions:
1. Recording the prevalence of infants with 46,XX-CAH and virilization as well as suspected DSD before birth and during the first 28 days of life
2. How the children were noticed and description of the phenotype (external genitalia)
3. Were genetic tests requested and if so, what tests and results, if any?
4. Where referrals made to specialised centres/specialists and if so, what type of centre/specialist.

Case definition:
Infants with 46,XX-CAH and virilisation, as well as with DSD (according to the German AWMF guideline variants of sex development [2], excluding Ullrich-Turner and Klinefelter syndrome) with a date of birth in the survey period and first diagnosis of DSD within the first 28 days of life defined as follows:

- a discrepancy between the prenatally determined karyotype and genital findings
- after birth, a genitalia that is not clearly male or female
- a female phenotype with enlarged clitoris, posterior fusion of the labia majora, urogenital sinus or inguinal/labial resistance
- Severe hypospadias (penoscrotal or perineal)
- 46,XX-CAH with viralised genitalia
- ICD 10 Chromosomal DSD: Q93.3, Q99.8, Q99.0
- ICD 10: 46,XY DSD: Q99.1, Q56.1, Q97.3, Q56.0, Q56.1, Q56.3, E34.5, E34.51, E34.59, Q54.2, Q54.3, E25.08
- ICD 10 46,XX DSD: Q99.1, Q56.0, E25.00, E25.08, E25.9, E25.8, Q87.8, 52.4

Estimate of the number of cases:
In recent years, around 780,000 children have been born in Germany each year. The assumed prevalence of a DSD diagnosis is approx. 1:4500 newborns. This means that approx. 170 children per year can be expected. This already includes the approx. 30 children with 46,XX-CAH, not the newborns with severe hypospadias

Logistics:
Please report all patients with DSD according to the above case definition. After reporting, the ESPED office will send out a questionnaire with questions on the clinic, phenotype, karyotype, genotype and follow-up care.

Literature:

1. https://dserver.bundestag.de/btd/19/279/1927929.pdf
2. Variations of sex development: The first German interdisciplinary consensus paper. Krege S, Eckoldt F, Richter-Unruh A, Köhler B, Leuschner I, Mentzel HJ, Moss A, Schweizer K, Stein R, Werner-Rosen K, Wieacker P, Wiesemann C, Wünsch L, Richter-Appelt H.. J Pediatr Urol. 2019 Apr;15(2):114-123. doi: 10.1016/j.jpurol.2018.10.008.