# Birth Weight in Different Aetiologies of Disorders of Sex Development

Poyrazoglu S[1], Darendeliler F[1], Ahmed SF[2], Bryce J[2], Jiang J[2], Rodie M[2], Hiort O[3], Hannema SE[4], Bertelloni S[5], Lisa L[6], Guran T[7], Hughes IA[8], Cools M[9], Chatelain P[10], Claahsen-van der Grinten HL[11], Nordenstrom A[12], Holterhus PM[13], Köhler B[14], Niedziela M[15], Krone N[16]

[1]Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey, [2]University of Glasgow, Glasgow, United Kingdom, [3] University of Lübeck, Lübeck, Germany, [4] Leiden University Medical Center, Leiden, Netherlands, [5] University Hospital Pisa, Pisa, Italy,[6] Institute of Endocrinology, Prague, Czech Republic, [7] Marmara University, Istanbul, Turkey, [8] University of Cambridge, Cambridge, United Kingdom, [9] University Hospital Ghent, Ghent University, Ghent, Belgium, [10] University Claude Bernard Lyon 1, Lyon, France, [11] Radboudumc Amalia Children's Hospital, Radbound University Medical Center, Nijmegen, Netherland, [12] Karolinska Institute, Stocholm, Sweden, [13] University Hospital Schleswig-Holstein, Kiel, Germany, [14] University Children's Hospital, Charite, Humboldt University, Berlin, Germany, [15] Poznan University of Medical Sciences, Poznan, Poland, [16] Center for Endocrinology, Diabetes and Metabolism, University of Birmingham, United Kingdom

## Background:

It is well known that boys are heavier than girls at birth. Causes of this difference are thought to originate from the Y chromosome and as a result of androgen action. Although some studies showed that sex dimorphism in size at birth is dependent of foetal androgens, one study reported that it is not generated by action of androgens.

## Aims and Objectives:

To determine birth weight(BW) of children in different aetiologies of Disorders of Sex Development (DSD) and evaluation of BW difference between 46,XX and 46,XY patients

Methods: Data regarding diagnosis, BW, karyotype and associated anomalies were gathered from the International DSD Registry (www.I-DSD.org). Because gestational ages of cases were not accessible in the registry, the clinicians in the registry were asked to report gestational ages. Small for gestational age (SGA) was defined as BW <-2 SDS. Cases were evaluated according to disorder classification in I-DSD as disorders of gonadal development, androgen synthesis, androgen excess, androgen action, and nonspecific disorder of undermasculinisation, Leydig cell defect, persistent müllerian duct and others. BW was expressed as SDS according to national standards for each country. Difference of BWSDS according to karyotype in groups and effect of presence of an androgen receptor gene (AR) mutation to BWSDS in androgen action group were evaluated.

Results are reported as median and IQR, and Mann-Whitney U test was used to evaluate difference between BWSDS. The proportions of other anomalies beyond the genitourinary system according to karyotype and BW were compared using Fisher's exact test. Two-tailed p values were calculated. Statistical significance was taken to be $p<0.05$.

## Results:

Of 460 accessible cases with BW and clinicians reported gestational ages of 295 cases. 246(83.4%) were 46,XY and 49(16.6%) were 46,XX. SGA was detected in 46 cases(15.6%), All SGA cases had 46,XY karyotype. Analysis of these BWSDS in the different diagnostic groups did not reveal any significant differences between 46,XX and 46,XY cases (Table 1).

BWSDS was substantially higher in the AR mutation-positive cases than in the AR mutation-negative cases (Table 2, p=0.03). Proportions of SGA were significantly lower in the AR mutation-positive cases compared with AR mutation-negative cases (Table 2, p=0.025).

Other anomalies beyond the genitourinary system were more frequent in SGA cases than appropriate for gestational age cases (respectively 32.6%, 10.8%, p=0.0001) and in 46,XY group than 46,XX group (respectively 15.8%, 6.1%, p=0.01).

**Table 1: Comparison of birth weight SDS of 46,XX and 46,XY cases according to disorder classification in I-DSD**

| Disorder Type | 46,XX /46,XY (n) | Birth Weight (gram) [Median(IQR)] | | P |
|---|---|---|---|---|
| | | 46,XX | 46,XY | |
| Gonadal Development | 8/26 | -0.36 (-0.94 / 0.93) | -0.48 (-1.34 / -0.10) | 0.28 |
| Androgen Synthesis | 10/42 | 0.08 (-0.68/0.39) | -0.56 (-1.18 / 0.21) | 0.10 |
| Androgen Excess | 29/18 | 0.03 (-0.48 /1.07) | -0.03 (-0.69 / 0.67) | 0.51 |
| Androgen Action | 0/117 | - | -0.98 (-1.97 /-0.16) | - |
| Nonspecific Disorder of Undermasculinisation | 0/25 | - | -1.24 (-2.25/0.36) | - |
| Leydig Cell Defects | 0/8 | - | -0.98 (-1.34/0.95) | - |
| Persistent Müllerian Duct | 0/2 | - | -0.86 and -0.16 | - |
| Other | 2/8 | -0.79/0.06 | -0.61 (-0.92/0.71) | - |

**Table 2: Evaluation of androgen action group according to presence of an androgen receptor gene mutation**

| | AR mutation-positive* N:15 | AR mutation-negative* N:54 | p |
|---|---|---|---|
| Birth Weight (gram) [Median(IQR)] | -0.92 (-1.91/0.55) | -1.83 (2.71/-0.69) | 0.03 |
| Proportion of SGA (%) | 13.3 | 44.4 | 0.025 |

*Results of 9 patients (1 AR mutation-positive, 8 AR mutation-negative)patients have been reported previously (*Lek N, Miles H, Bunch T, Pilfold-Wilkie V, Tadokoro-Cuccaro R, Davies J, Ong KK, Hughes IA. Low frequency of androgen receptor gene mutations in 46 XY DSD, and fetal growth restriction. Arch Dis Child 2014 ;99:358-61*)

## Conclusions:

- Size at birth in both karyotypes seems unlikely to be dependent on foetal androgens.
- SGA is more frequent in infants with AR mutation-negative compared with infants with AR mutation-positive
- Syndromal forms of DSD with multi-system involvement are more likely to be SGA.

Disclosure :The authors have nothing to disclose.


DOI: 10.3252/pso.eu.54espe.2015