

# GONADAL OUTCOME IN 17BETA-HSD AND 5ALPHA-REDUCTASE DEFICIENCY

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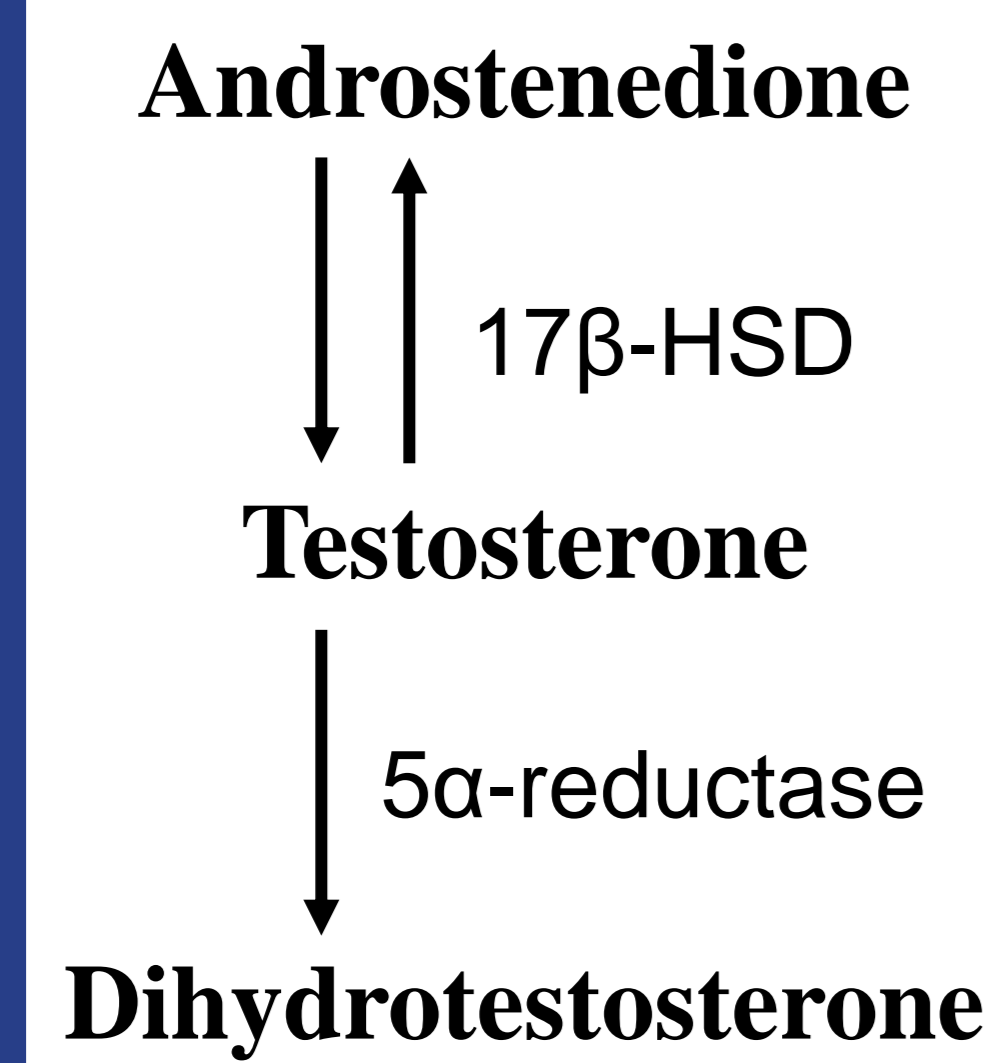
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## INTRODUCTION

5 $\alpha$ -reductase type 2 deficiency (5 $\alpha$ -RD) and 17 $\beta$ -HSD type 3 deficiency (17 $\beta$ -HSDD) are rare differences/disorders of sex development (DSD) in which impaired function of steroidogenic enzymes causes undervirilisation in individuals with a 46,XY genotype.

## AIM

We aim to increase the limited knowledge on long-term gonadal function and gonadal pathology in these conditions.



## METHOD

Eligible individuals were identified using the International DSD (I-DSD) Registry.

### Inclusion-criteria:

- Current age  $\geq 16$  years
- Genetically conformed diagnosis
- Data available on gonadal outcome

### Data collection:

- Information on laboratory results, pathology results, hormone treatment and surgeries
- Representative block(s), slides or images of gonadal tissue were requested to allow a uniform analysis of the gonadal tissue.

## RESULTS

A total of 36 subjects from 10 different centres were included in this study. Their characteristics are shown in **Table 1**.

### GnRHa therapy

GnRHa therapy was initiated in four female subjects of whom three with 17 $\beta$ -HSDD (**Table 1**).

- One individual underwent gonadectomy after one year of GnRHa, at age 14 years.
- In one individual, treatment was discontinued after several months as the subject decided to change to the male gender at age 14 years.
- In two individuals GnRHa was initiated at the age of 11 and 14 years, gonadectomy is planned after the age of 18 years.

### Gender Change

Gender change occurred in eight individuals at a median age of 19 years (range 15 – 25).

## CONCLUSIONS

- A significant percentage (22%) of individuals with 5 $\alpha$ -RD and 17 $\beta$ -HSDD changed gender, mostly in late adolescence/early adulthood.
- To prevent virilisation before making a definitive decision about gonadectomy, treatment with GnRHa is being used.
- When gonads are left in situ, testosterone levels are in the low-normal range in postpubertal individuals.
- Germ cell (pre)malignancies seem uncommon in these patients, but central reassessment of gonadal material is ongoing to confirm this finding.

Together, these data support a conservative approach towards definitive sex assignment, genital surgery and gonadectomy early in life in these conditions.

	5 $\alpha$ -RD	17 $\beta$ -HSDD
<b>Subjects, n</b>	18	18
<b>Age first presentation, y (IQR)</b>	6.5 (4.8-15.5)	7.5 (2.8 – 16.8)
<b>Age diagnosis, y (IQR)</b>	11.8 (5.0 – 16.3)	13.5 (7.5 – 19.0)
<b>EGS first presentation, (range)</b>	7.0 (2.5 – 11.0)	2.0 (0.5 – 6.0)
<b>Female gender of rearing, n</b>	11 (61%)	18 (100%)
<b>Gender change, n</b>	4 (22%) FtM 1 (6%) MtF	3 (17%) FtM
<b>Hormone therapy, n</b>	1 (6%) GnRHa 5 (28%) DHT 6 (33%) Estrogen	3 (17%) GnRHa 0 (0%) DHT 13 (72%) Estrogen
<b>Gonadectomy, n</b>	6 (33%)	13 (72%)
<b>Age gonadectomy, y (IQR)</b>	10.0 (6.0 – 18.3)	8.0 (3.0 – 13.5)

**Table 1.** Characteristics of both groups. Data are presented as median (interquartile range) unless stated otherwise.

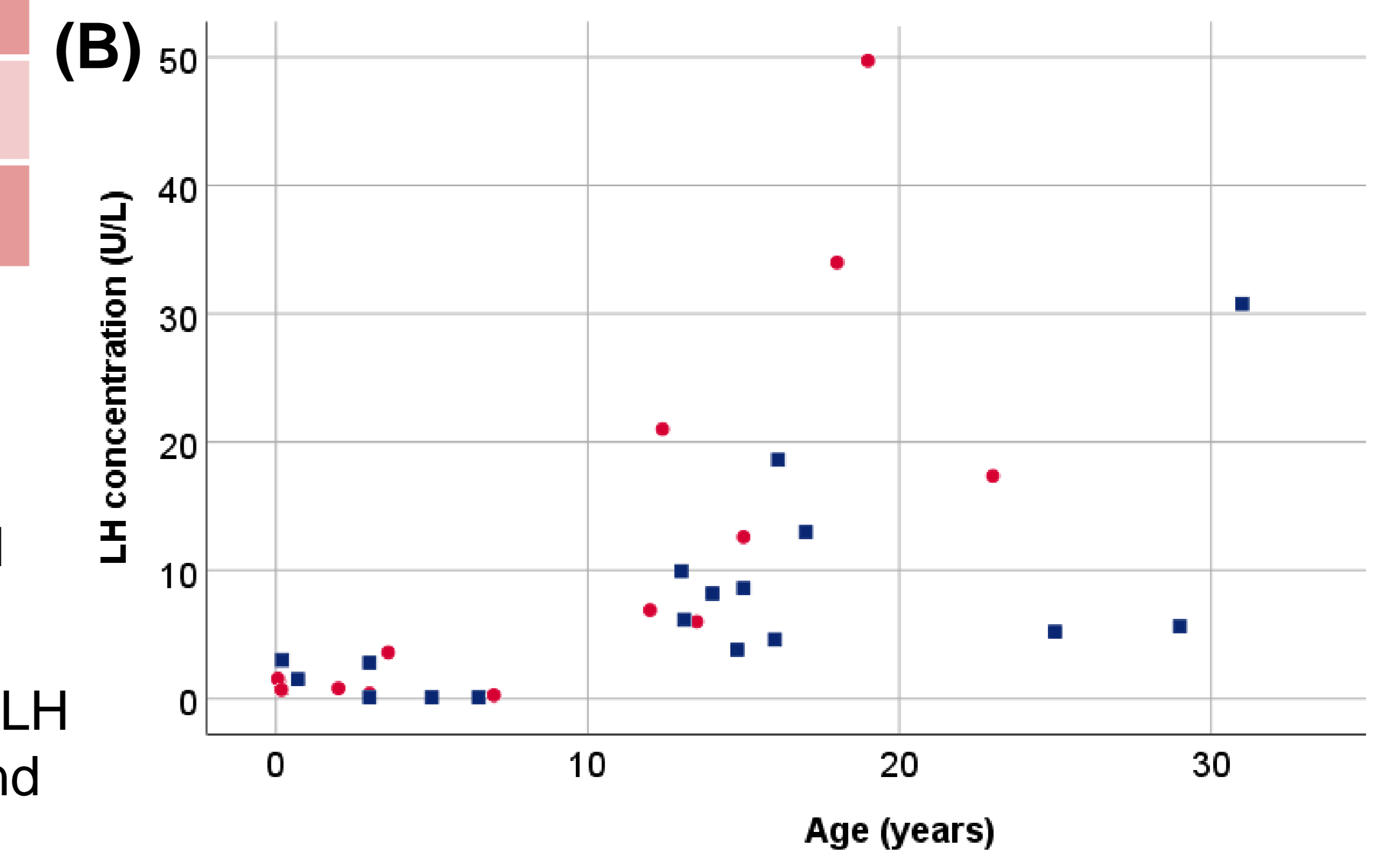
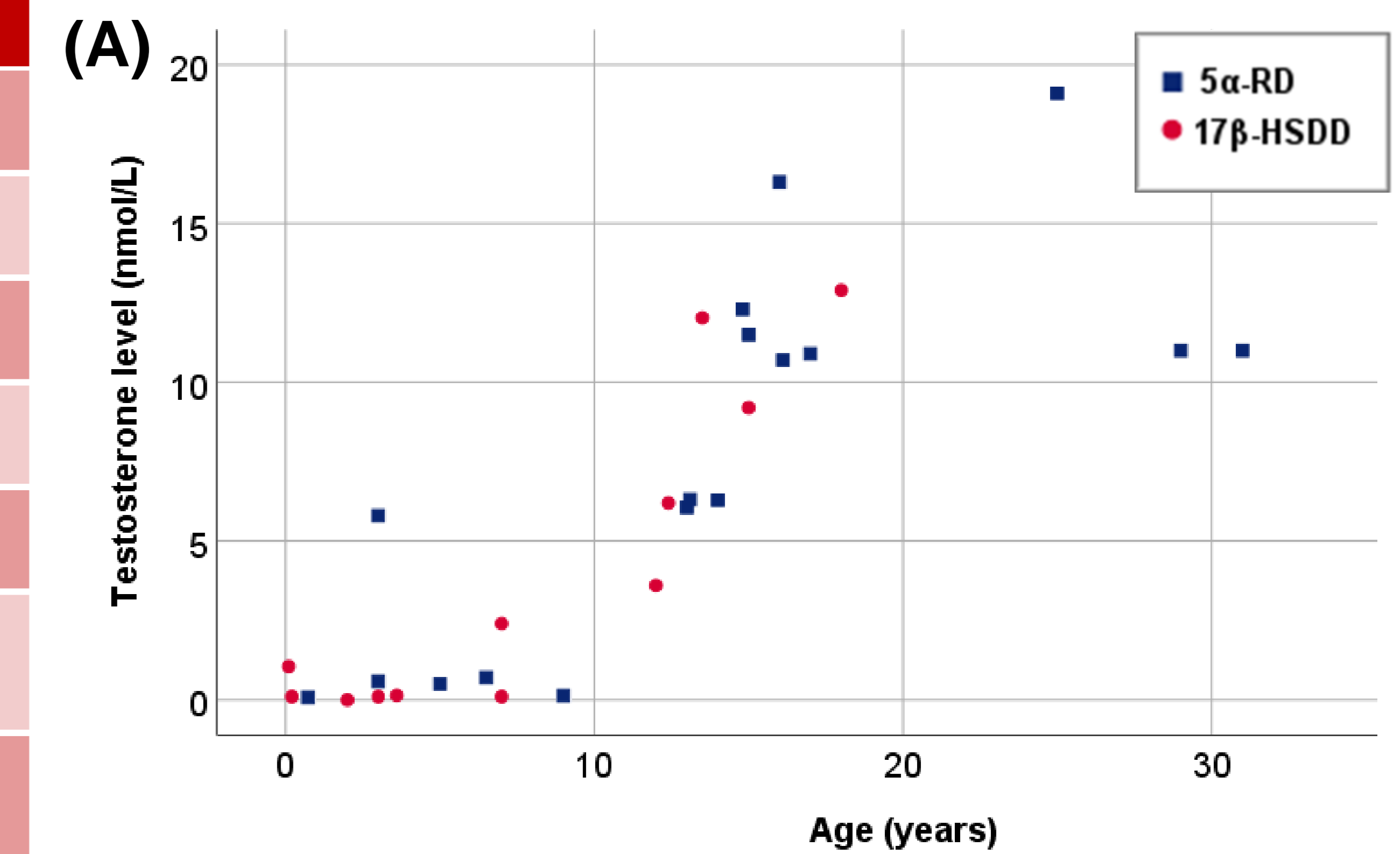
### Endocrine gonadal function

Pubertal/postpubertal individuals without treatment and/or gonadectomy had testosterone levels within the low-normal range, see **figure 1A**.

However, elevated gonadotrophins were common, especially in 17 $\beta$ -HSDD. LH levels are shown in **figure 1B**. Median FSH levels were 29 (range 2 – 75) and 8 U/L (2 – 61) in 17 $\beta$ -HSDD and 5 $\alpha$ -RD, respectively.

### Gonadal pathology

No (pre)malignancies were reported.



**Figure 1.** Testosterone (A) and luteinizing hormone (B) levels by age in individuals with 5 $\alpha$ -reductase type 2 deficiency (blue squares) and 17 $\beta$ -HSD type 3 deficiency (red dots) without hormone treatment and without / before gonadectomy.

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