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Authors have nothing to disclose

Purpose

With improvements in assays and the increasing need for non-invasive, out-patient based investigations, there is a renewed interest in the use of urinary gonadotrophins (UG) for assessing pubertal progress. This study aims to establish the correlation between serum and urinary LH and FSH in patients with pubertal disorders.

Methods

Retrospective evaluation of 36 patients undergoing investigation for: pubertal delay (9M, 6F), early puberty (1M, 5F), central precocious puberty (CPP) (2M, 8F) and disorders of gender identity (GID) (3M, 2F). Main population characteristics are summarized in Figure 1.

Median ages (range) for boys and girls were 14.9 yrs (7.8-17.3) and 9.5 yrs (4.3-18.4), respectively. Non-timed spot urine samples were collected for all cases, and 13 (5M, 8F) were receiving GnRH-agonist (GnRH-a) treatment. Matched serum basal gonadotrophins were available in 24 cases (12M, 12F). Urinary results were compared to reference values for healthy children (Mc Neilly et al. 2012). UG were measured by chemiluminescent microparticle immunoassay and corrected for urinary creatinine.

Figure 1: Main population characteristics

36 patients: 15 M;21 F 52 random urine samples collected					
Main reason of attendance	Pubertal delay	Early puberty	CPP	GID	On treatment
Number of patients	M 9 F 3	M 1 F 5	M 2 F 10	M 3 F 3	M 3+2 F 1+7
Age (yrs)	14.8 (12.3; -17.3) \\ 16.4 (12.7; 18.4)	7.8 \\ 8.5 (7.3 ; 9.5)	10.4 (8.9; 11.9) \\ 8.6 (4.3;10.7)	15.2 (14.9;15) \\ 14.1 (13.5;14.7)	
Height SDS	-1.4 (-3.3; 0.8) \\ -1.7 (-2.6; -1.2)	1.5 \\ 2.6 (0.5;4.6)	2.3 (1.4;3.2) \\ 1.6 (-1.4; 2.7)	0.3 (-0.6;1.1) \\ 1.0 (-1.4; 1.2)	
Weight SDS	-1.3 (-3.4; 2.0) \\ -2.3 (-3.2; -1.9)	2.4 \\ 2.5 (2.2;2.9)	1.7 (1.5;1.8) \\ 1.6 (0.8; 3.1)	1.2 (-0.1;1.9) \\ 2.6 (0.3; 3.1)	
BMI SDS	-0.268 (-1.3-2.5) \\ -2.8 (-3.0; -0.3)	2.3 \\ 2.5 (1.6;3.2)	1.0 (0.7;1.2) \\ 1.8 (0.03; 3.0)	0.4 (0.4;1.8) \\ 2.3 (1.3; 2.7)	
Bone Age-CA (yrs):	-1.7 (-3.5; 0.2) \\ -2.8 (-3.0; -0.3)	1.9 \\ 3.4 (0.9;3.4)	6.3# \\ 1.9 (1.1; 3.1) # available only for one of the two patients	Not Available	

Results

Comparisons between UG values of our population and previous reference data for pre-pubertal and pubertal people are shown in Figures 2a and 2b and summarized in Table 1. Overall, the median levels of UG increased with pubertal development and decreased with pubertal suppression both for male and female.

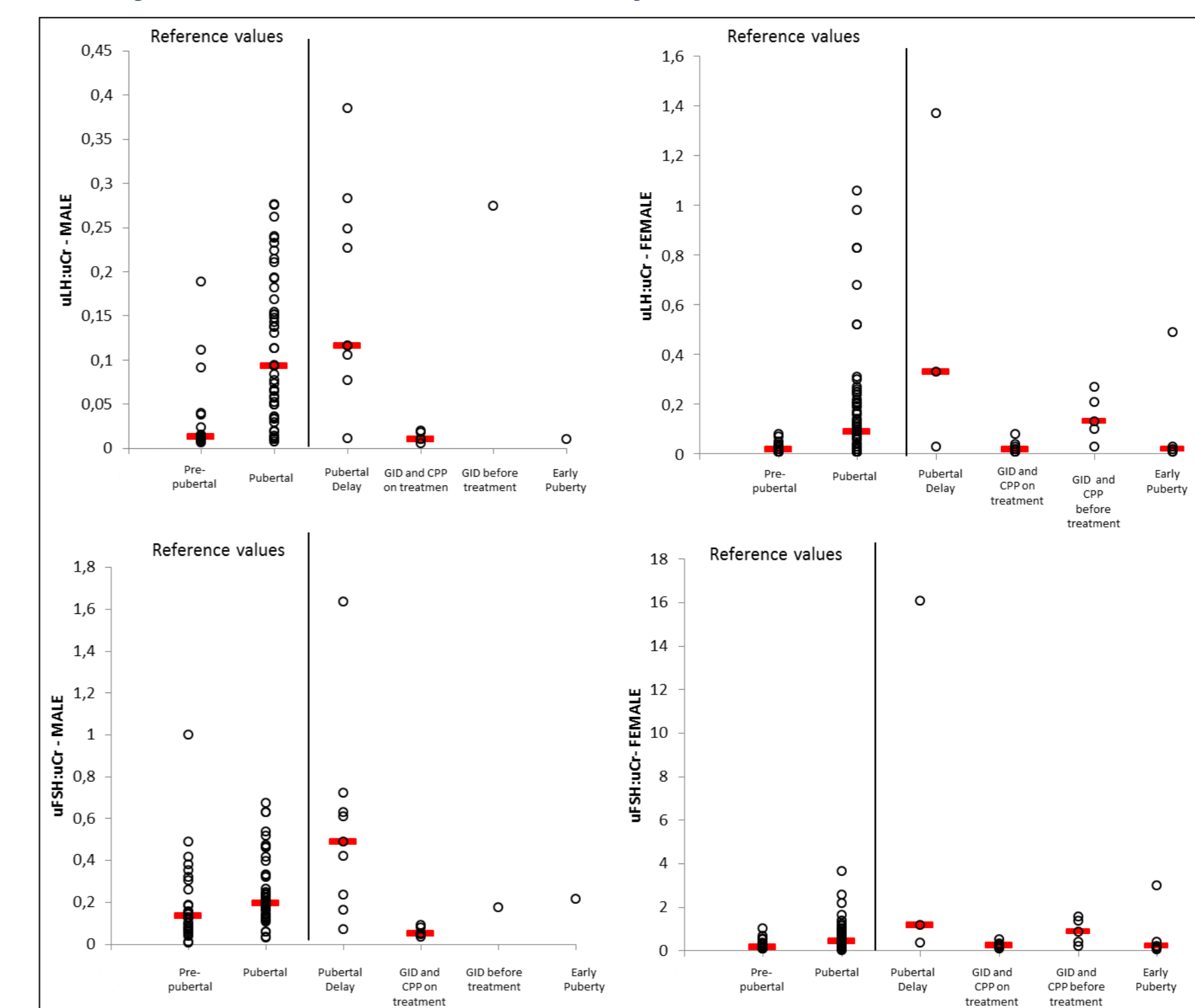
	MALE			FEMALE		
	ULH:UCr	UFSH:UCr	ULH/UFSH	ULH:UCr	UFSH:UCr	ULH/UFSH
Pre-pubertal [#] vs Pubertal [#]	$p = 0.0001$	$p = 0.018$	$p = 0.0001$	$p = 0.003$	$p = 0.006$	$p = 0.036$
Pre-pubertal [#] vs Pubertal delay	$p = 0.0001$	$p = 0.006$	$p = 0.005$	$p = 0.03$	$p = 0.03$	$p = 0.45$
Pubertal [#] vs Pubertal delay	$p = 0.12$	$p = 0.023$	$p = 0.279$	$p = 0.16$	$p = 0.15$	$p = 0.51$
Pre-pubertal [#] vs GID and CPP on Treatment	$p = 0.569$	$p = 0.027$	$p = 0.087$	$p = 0.53$	$p = 0.93$	$p = 0.61$
Pubertal [#] vs GID and CPP on Treatment	$p = 0.004$	$p = 0.003$	$p = 0.009$	$p = 0.012$	$p = 0.025$	$p = 0.064$
Pre-pubertal [#] vs GID and CPP before treatment	-	-	-	$p = 0.01$	$p = 0.021$	$p = 0.35$
Pubertal [#] vs GID and CPP before treatment	-	-	-	$p = 0.42$	$p = 0.25$	$p = 0.65$
Pre-pubertal [#] vs Early puberty	-	-	-	$p = 0.83$	$p = 0.99$	$p = 0.55$
Pubertal [#] vs Early puberty	-	-	-	$p = 0.3$	$p = 0.26$	$p = 0.39$

#: Reference data of healthy controls

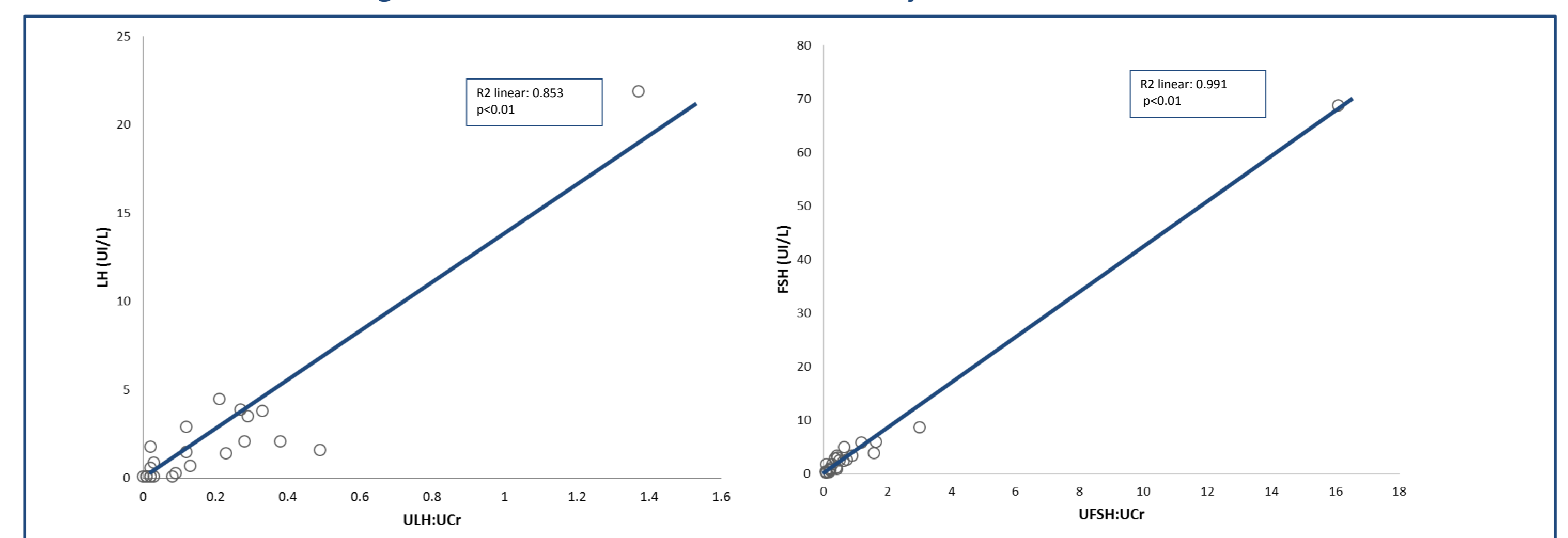
Table 1: Summary of Mann-Whitney U test results, comparing different populations both for males and females (values are considered as statistically significant when $p < 0.05$)

Results

Figures 2a and 2b: Comparison between reference values and patients results both for males and females: median values represented with red line

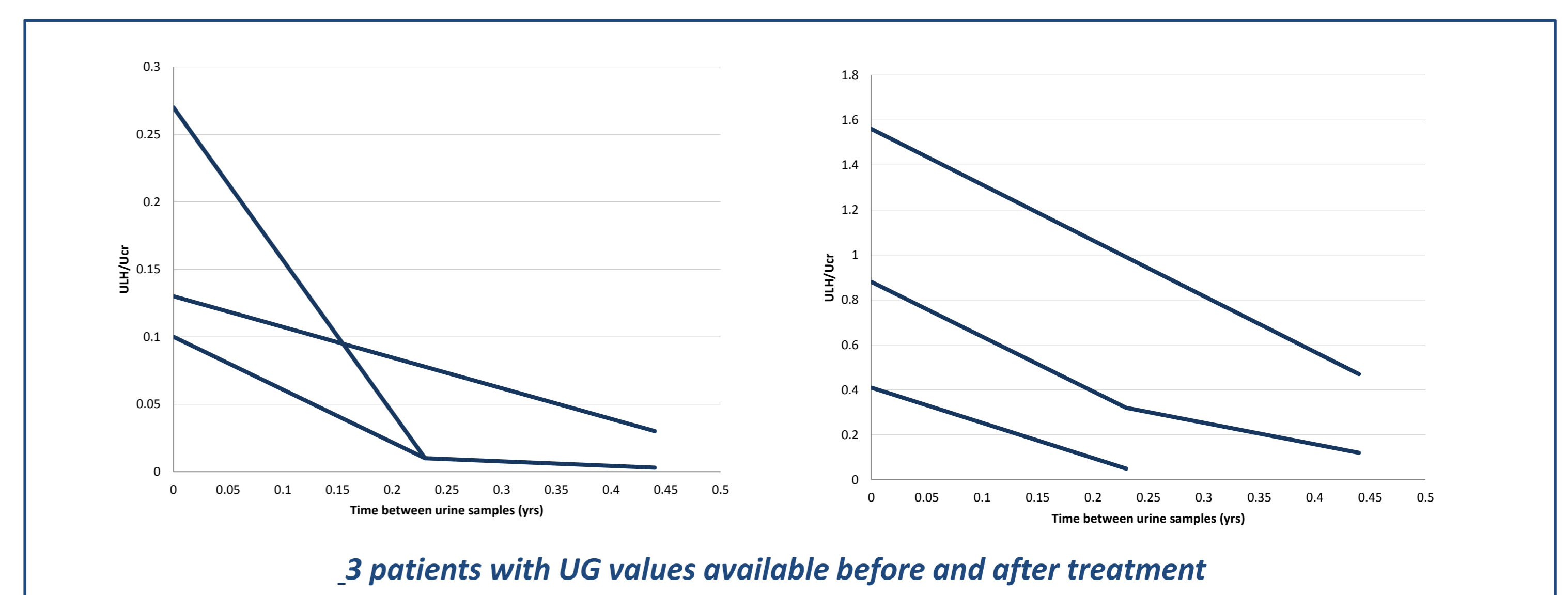


Figures 3: Correlation between urinary and blood LH and FSH

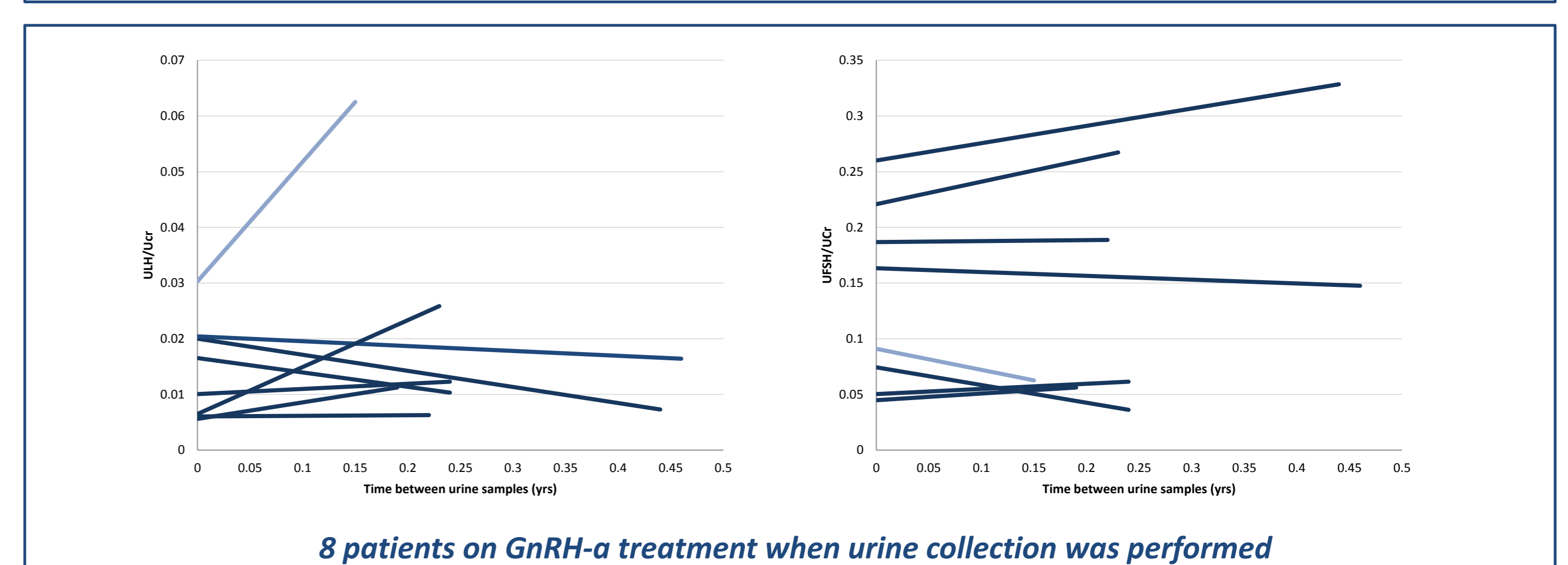


Significant associations were found both for LH and FSH even after removing outlier: coefficient of correlation between ULH:UCr and Serum LH was 0.866 while between UFSH:UCr and Serum FSH 0.905

Figures 4 and 5: Change in ULH:UCr and UFSH:UCr ratios during GnRH-a treatment



3 patients with UG values available before and after treatment



8 patients on GnRH-a treatment when urine collection was performed

There is a rapid UG decrease after initiation of GnRH-a, while during treatment UG remain stable. Only one patient with CPP had rise of ULH:UCr: she was at the end of her treatment, with clinical signs of pubertal progression (light blue patient).

Conclusions

These preliminary data suggest that UG reflect serum gonadotrophin concentrations and the finding of low UG in patients on GnRH-a therapy suggest that this test may represent a useful non-invasive method of assessing and monitoring effectiveness of GnRH-a therapy.

References

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- Carel JC, Eugster EA, Rogol A, Ghizzoni L, Palmert MR. Consensus Statement on the Use of Gonadotropin-Releasing Hormone Analogs in Children. *Pediatrics* 2009; 123: e752-62