

INHIBIN B IN THE DIAGNOSIS OF DELAYED PUBERTY

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Background

The differential diagnosis between isolated hypogonadotropic hypogonadism (HH) and constitutional delay of puberty (CDP) is very difficult in clinical practice. Existing tests are not 100% accurate. Perhaps AMH and inhibin B levels can offer some diagnosis alternatives. The level of inhibin B increases 12 months before the clinical onset of puberty and it raises progressively from G1 to G3 Tanner stage.

Aim

To evaluate the utility of inhibin B level in differentiating between CDP and HH in boys.

Materials and methods

Retrospective study - 18 subjects, all boys G1 Tanner stage – 10 CDP and 8 HH (4 - isolated HH, 4 -panhypopituitarism).

We studied :

-auxometrical parameters- height, weight, genital stage, testicular volume.

-laboratory parameters: bone age, basal FSH, LH, testosterone, AMH, inhibin B levels and stimulated FSH, LH and testosterone level after soluble sc Triptorelin (100 mcg/sm).

The method used to determine FSH, LH, testosterone was ECLIA and for AMH and inhibin B - Gen II ELISA kit.

Statistical analysis: KRUSKAL Wallis test, Pearson correlation and the ROC curve.

Results and discussion

Parameters with statistically significant differences between the two groups.

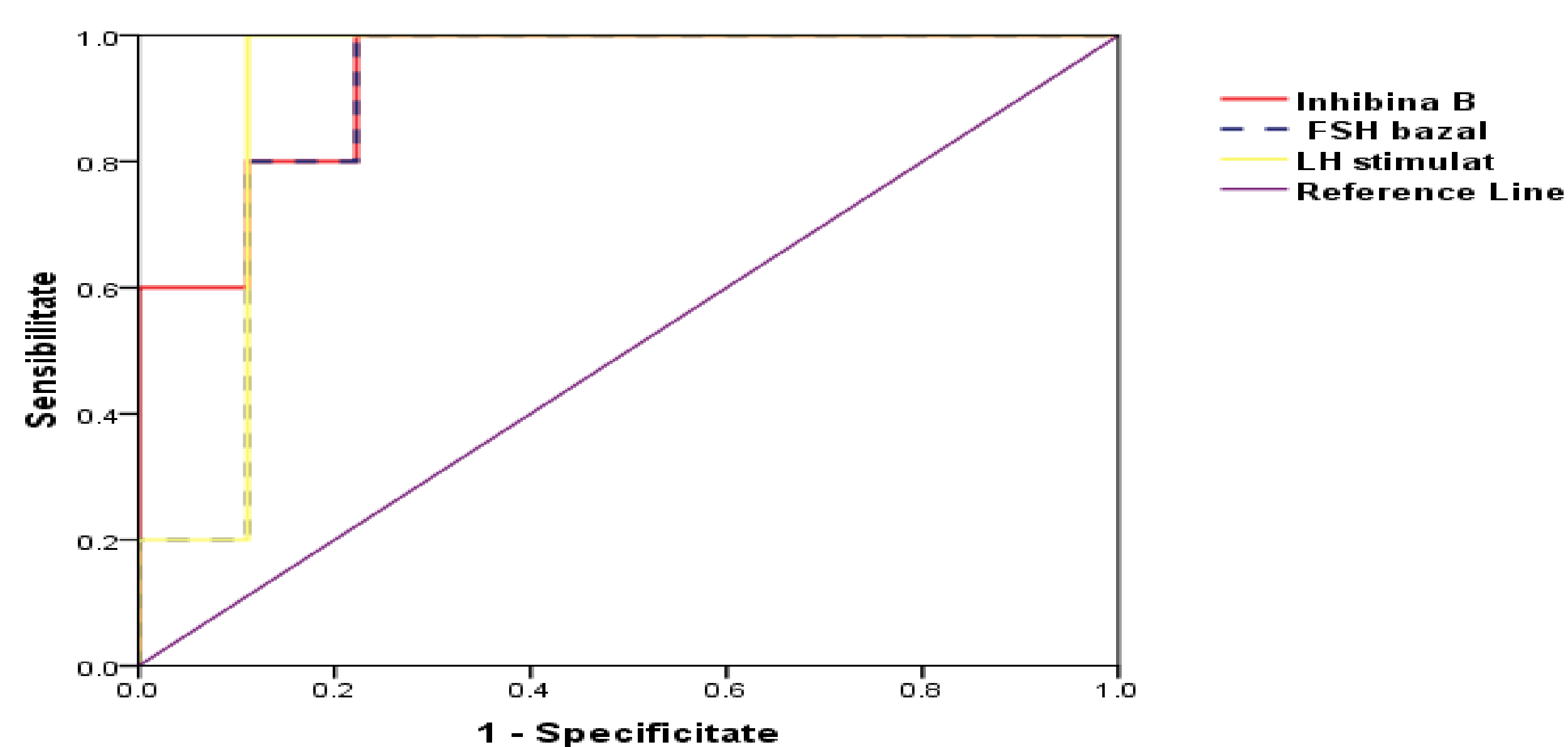
The subjects with HH had lower levels of inhibin B, basal FSH and stimulated LH. So, the level of inhibin B correlates with the values of basal FSH and stimulated LH.

The level of AMH was also lower in subjects with HH, but with no statistical significance.

	HH (n=8)		CDP (n=10)		p
	media± DS	Range	media± DS	Range	
Inhibin B (pg/ml)	31,5±20	13,8- 71,55	98,8±43	31,8-195,6	< 0,01
Basal FSH (mIU/ml)	0,77±0,6	0,19- 2,2	2,5± 1,2	0,2- 4,2	< 0,05
LH – 4 h (mIU/ml)	1,12± 1	0,1 – 3,03	13 ± 8	0,21-30,8	< 0,05

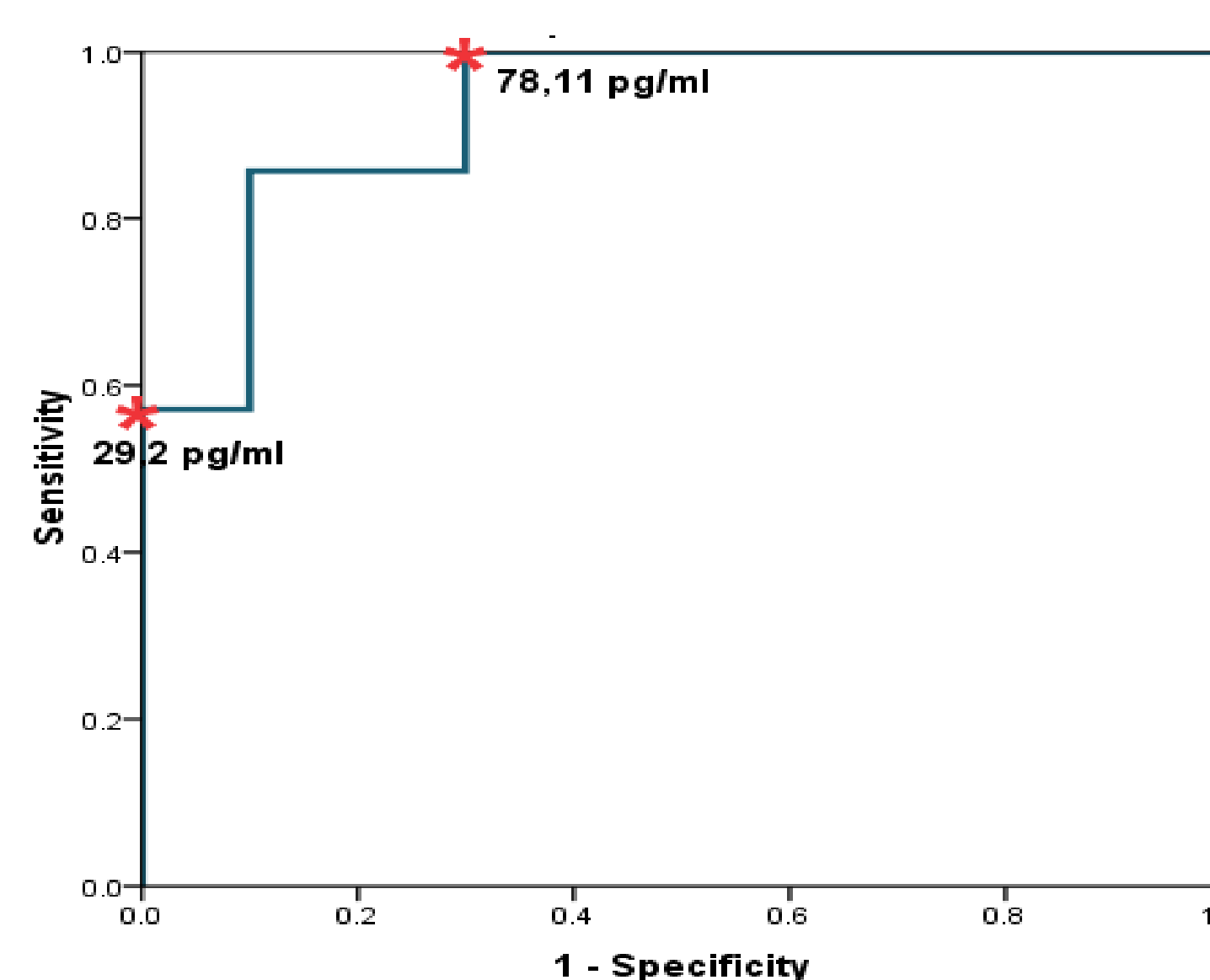
ROC curve analysis

	Threshold value	Specificity for HH	Sensitivity	Diagnostic accuracy
Inhibin B (pg/ml)	< 29,2	100 %	57%	83,3%
LH 4 h (mIU/ml)	< 2,5	89%	80 %	83,3%
Basal FSH (mIU/ml)	< 0,97	89 %	80 %	77,7%

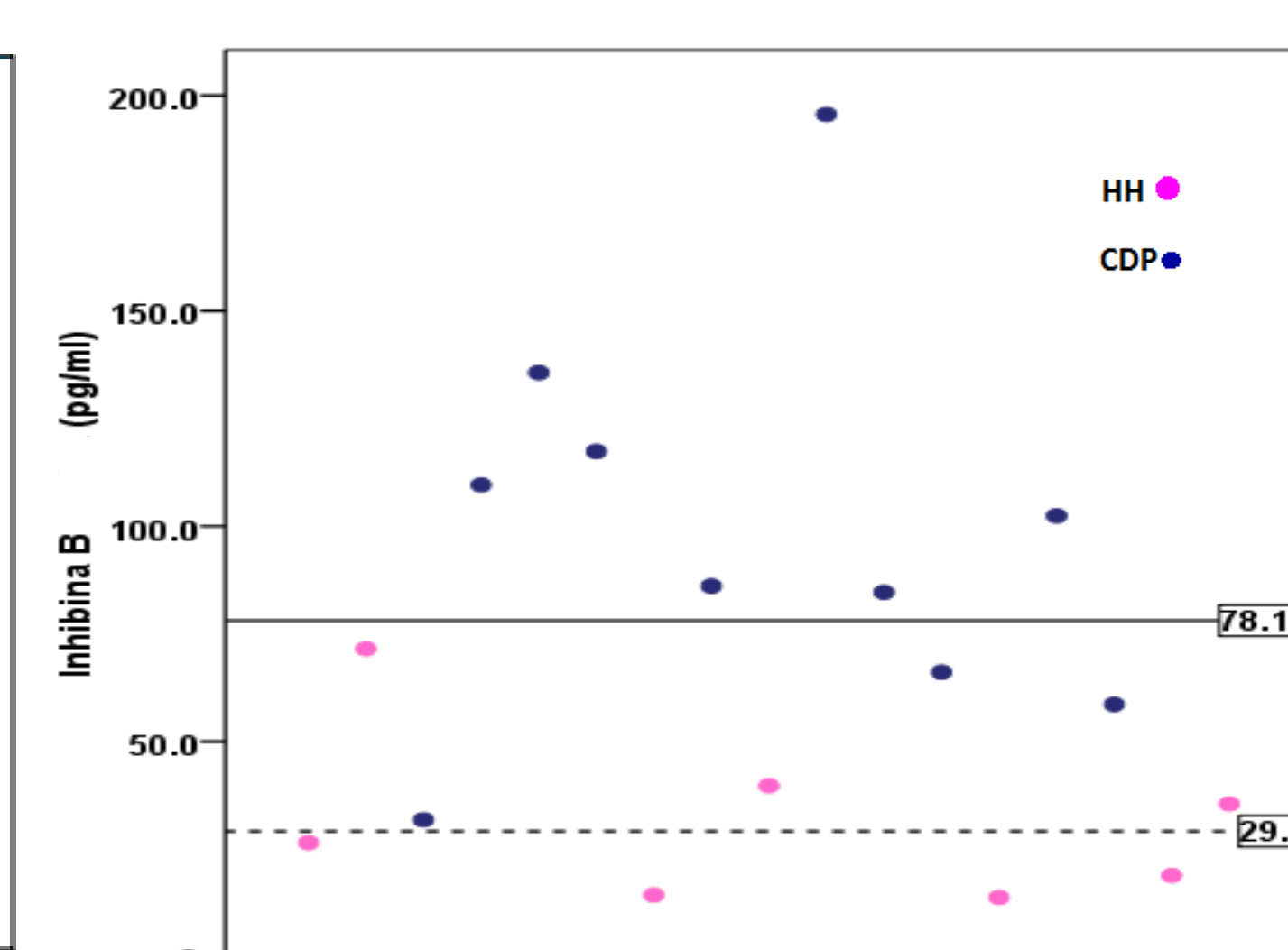


Parameter	AUC	p	95% CI	
Inhibin B	0,933	0,009	0,804	1,063
Basal FSH	0,889	0,02	0,706	1,072
Stimulated LH	0,911	0,014	0,738	1,084

ROC curve for inhibin B



Inhibin B values in CDP and HH subjects



The area under the ROC curve showed the high predictive value of inhibin B for HH subjects (AUROC=0.933), with p=0.009. So, a level of inhibinB under 29.2 pg/ml has 100% specificity for HH and a level above 78.11 pg/ml detects in 100% cases the subjects with CDP. In our groups the two threshold values of inhibin B differentiate in 66.6% of cases the subjects with CDP from those with HH.

Conclusions

The value of inhibin B can be an efficient marker for pubertal onset and it can differentiate HH from CDP in almost 67% of cases so it can be used as a first line test for the differential diagnosis between the two conditions.

Moreover, it aids in cost reduction, since Triptorelin sc testing will only need to be performed for patients with inhibin B values in the grey zone (29.2-78.1 pg/mL).