# KISSPEPTIN LEVELS IS A NEW DIAGNOSTIC APPROACH OF HYPOGONADOTROPIC HYPOGONADISM IN BOYS

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**Background.** In hypogonadotropic forms of delayed puberty (DP), hypophyseal follicle-stimulating and luteinizing hormones, normally released with GnRH stimulation, are detected low. Since kisspeptin (KP) is a strong stimulant of GnRH neurons, it is considered to have a role in DP etiology. It may be hypothesized that abnormal plasma levels of KP
are indicative of DP.

**Aim.** Evaluation and comparison of plasma KP levels in boys of prepubertal age, with normal puberty and diagnosed primary hypogonadotropic forms of DP.

**Methods.** A case-control study design with three groups of patients was used. The study comprised 22 boys with hypogonadotropic DP (age 14-17 years, group1), 25 boys with normal puberty, Tanner stage III-V (age 14-17 years, (group2), and 28 pre-pubertal boys (age 6-9 years, group3). All patients of group1 were presented with a testicular
volume ≤4 ml and a Tanner stage 1 at the time of study, and they had serum early morning LH values < 0.1 IU per liter; serum FSH values < 0.2 IU per liter, and total serum TST < 0.5 nmol per liter. Laboratory investigations were aimed to define plasma KP level. Plasma KP concentration was determined by enzyme-linked immunosorbent assay (ELISA) using Elisa Kit for Kisspeptin 1 (KISS1) (CEC559Hu) (Cloud-Clone Corp).
Descriptive and analytical statistics were used in data analysis. The Mann-Whitney U test, the Kurskal-Wallis test (non-parametric analogue of one-way ANOVA) with Dunn's pairwise between-group posttests, two-way ANOVA andchi-square test with Yates' correction or Fisher exact test where appropriate were used in data analysis.

**Results.** Statistically significant difference was found for the overall distribution of the plasma KP values across different groups (Kruskal-Wallis H = 21.95, P = < 0.001). (Fig1.) The highest values were found in the DP group (median: 45.0 pg/mL).
Median values in the pre-pubertal boys and in the normal pubertal adolescents were equal to 13.8 pg/mL. No statistically significant difference was found for plasma KP levels in the DP boys who had either positive or negative response to Triptorelin stimulation test (Fig2.). ROC curve analysis was performed. The area under the ROC curve (AUC) was equal to 0.854 (95% CI: 0.720 to 0.940), enabling rejection of the null-hypothesis (area of 0.5) (p < 0.0001) (Fig3.). The criterion value that ensured optimal balance between sensitivity and specificity was equal to 16.9 pg/mL. This corresponds to the value of the Youden index J equal to 0.6473, test sensitivity equal to 72.73, and test specificity equal to 92.0.
**Conclusion.** Plasma KP level exceeding 16.9 pg/mL was a reliable predictor of hypoganadotropic DP (sensitivity = 72.7, specificity = 92.0).

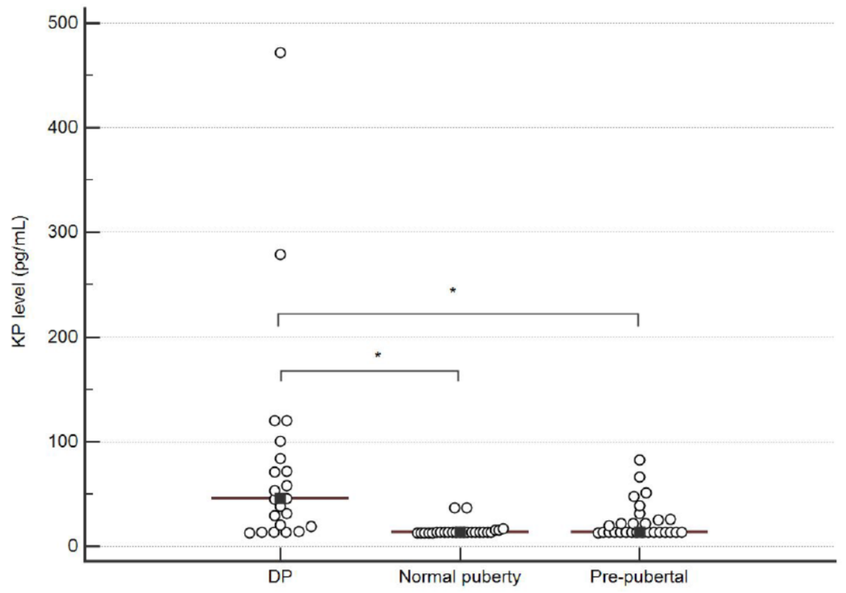


Figure 1. Plasma kisspeptin levels (pg/mL) in different patients groups. Horisontal marker lines correspond to the median values. DP – delayed puberty. * - p < 0.05

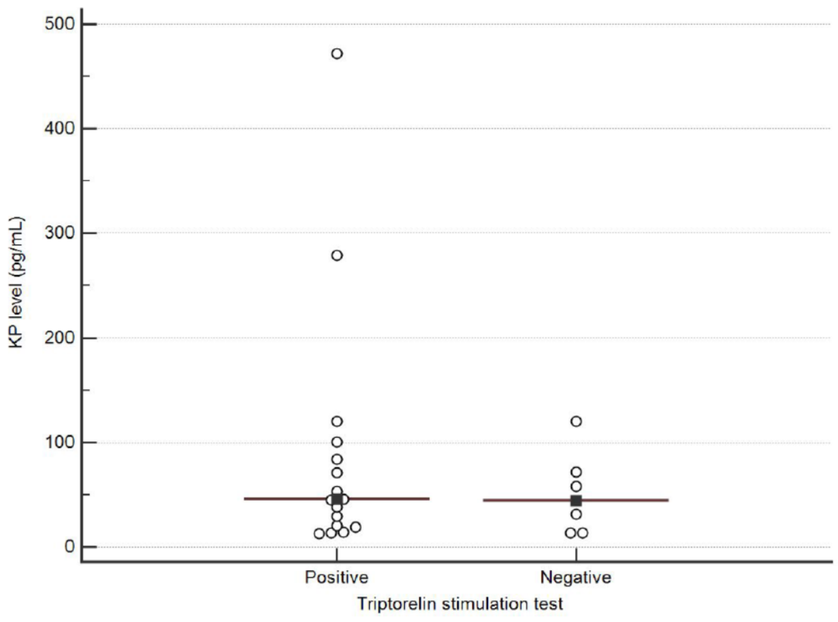


Figure 2. Plasma kisspeptin levels (pg/mL) in the DP boys with positive and negative responses to the Triptorelin stimulation test. Horisontal marker lines correspond to the median values.

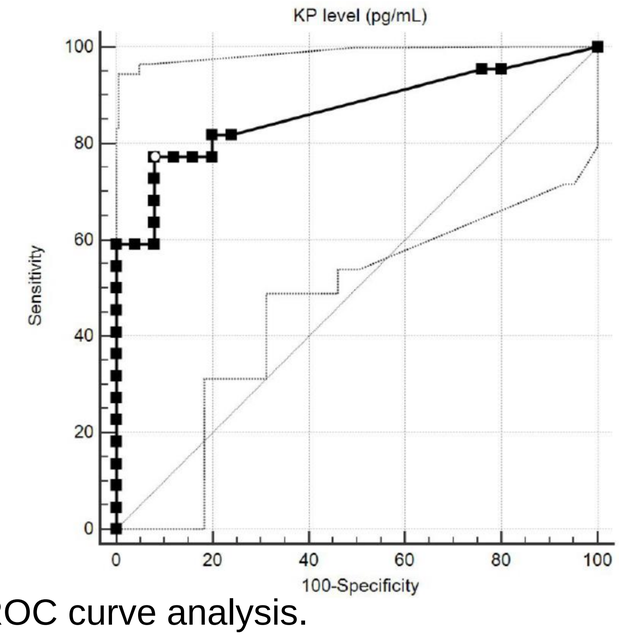


Figure 3. ROC curve analysis.