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Original Article

Predictive value of transabdominal pelvic ultrasonography for the diagnosis of central precocious puberty: A single-center observational retrospective study

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Highlights

- Pelvic ultrasonography serves as a rapid and reliable method for indirectly assessing the activation of the hypothalamic-pituitary-gonadal axis and can differentiate central precocious puberty (CPP) from premature thelarche and other causes of normal pubertal development.
- In our retrospective monocentric study, pelvic ultrasonography had a sensitivity of 91.17% and a specificity of 38.46% in differentiating CPP from premature thelarche.
- Despite our results, the gonadotropin-releasing hormone test remains the gold standard for diagnosing CPP, even though it is an invasive method.

Abstract. This single-center, observational, retrospective study aimed to evaluate the diagnostic accuracy of pelvic ultrasonographic parameters for detecting central precocious puberty (CPP) in a cohort of female pediatric patients undergoing gonadotropin stimulation tests. The study population consisted of 47 female patients with a suspicion of CPP. Thirty four out of 47 patients (72.34%) were subsequently diagnosed with CPP based on the current laboratory diagnostic criteria (LH peak > 5 IU/L). The ultrasonography results of 39 out of 47 patients (82.97%) were categorized as pubertal, while 31 out of 34 participants (91.17%) in the CPP group exhibited pubertal ultrasonography features. In 13 out of 47 girls (27.65%), a CPP diagnosis was ruled out; however, among these 13 patients, eight exhibited pubertal ultrasonography features suspicious of CPP. We observed a robust concordance between the GnRH test results indicative of pubertal activation and the presence of pubertal pelvic ultrasonographic features in 31 out of 34 children (91.17%). A significant correlation was found between ovarian volume and basal LH and LH/ FSH ratio, and also for basal LH, LH peak, LH/FSH ratio and peak LH/FSH ratio ($p = 0.026$, $p = 0.011$, $p = 0.031$, $p = 0.004$, respectively). Pelvic ultrasonography had a sensitivity of 91.17% and a specificity of 38.46% in differentiating CPP from premature thelarche.

Key words: central precocious puberty, pelvic ultrasonography, pediatric endocrinology

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Introduction

Precocious puberty is defined as the appearance of secondary sexual characteristics before the age of 8 yr in girls and 9 yr in boys. These limits correspond to a –2.5 standard deviation score (SDS) below the mean age of puberty onset (10.5 yr in females and 11.5 yr in males, respectively) (1). The classification of precocious puberty traditionally distinguishes between central and peripheral forms. Central precocious puberty (CPP), also termed gonadotropin-dependent precocious puberty or *true* precocious puberty, results from the premature maturation of the hypothalamic-pituitary-gonadal axis, leading to the development of secondary sexual characteristics such as the formation of mammary glands in females and enlargement of testicles in males (1), in line with the biological sex of the child. CPP is idiopathic in 80–90% of females (2, 3) but only in 25–80% of males (4), in whom it is more common to have an organic origin arising from lesions in the central nervous system. In recent years, there has been an increase in cases of CPP, coinciding with the SARS-CoV-2 pandemic (5), highlighting how, although idiopathic etiology remains the most frequent cause of CPP, stress and other exogenous factors might play a crucial role in the activation of the hypothalamic-pituitary-gonadal axis.

It is crucial to differentiate between benign pubertal developmental conditions, such as premature thelarche, and pubertal development related to activation of adrenal steroidogenesis, known as premature adrenarche (6, 7).

The diagnosis of CPP is challenging and relies on the medical history of the patient, progression to pubertal stage, bone age assessment (typically advanced), pelvic ultrasonography findings (revealing endometrial and ovarian stimulation), and hormonal assay results (8). Rapid identification of CPP is essential because, if left untreated, it leads to a reduction in the final body height attained at adulthood due to the premature fusion of growth plates (9). Baseline and stimulated gonadotropin levels are pivotal for diagnosis, with the GnRH stimulation test currently serving as the gold standard for CPP diagnosis (2); however, this test is undermined by various limitations (10), including the requirement for peripheral venous access, time constraints, and notably, variability in the interpretation of diagnostic results, which does not allow for homogeneous diagnoses across various centers. Indeed, the diagnostic cutoff for LH varies based on the consulted guidelines (11), ranging from a minimum of 3.3 IU/L up to 5–10 IU/L (2). Additionally, patients must undergo serial blood draws for gonadotropin measurements, although in most cases the LH peak is confirmed in the first sample taken 30 min after infusion (10). In a previous study, we highlighted the association between basal LH and peak gonadotropin levels during the GnRH test (9), demonstrating a higher sensitivity in the diagnosis of CPP despite low specificity. Therefore, it is crucial to integrate test data with auxological and radiological parameters to identify other clues for the diagnosis of pubertal activation.

Pelvic ultrasonography is a noninvasive, painless, inexpensive, and reliable tool for studying the pelvis in girls and could potentially represent a valid alternative to performing GnRH tests in patients suspected of having CPP. Pelvic ultrasonography serves as a rapid and reliable method for indirectly assessing the activation of the hypothalamic-pituitary-gonadal axis (12). The size and morphology of both the uterus and ovaries typically remain relatively stable from infancy until puberty (13), when they progressively increase in size and change their morphology (14–21). Many studies have indicated that girls with CPP exhibit an increase in uterine and ovarian volumes, along with alterations in uterine morphology (predominance of the fundus over the cervix) and the presence of ovarian follicles with diameters larger than 6 mm (18, 19), compared to those at a prepubertal age and girls with isolated premature thelarche (20, 30). However, upon statistical analysis of the diagnostic value of these sonographic findings, most studies have found that despite their robust specificity, the sensitivity was low, likely due to either the transabdominal approach or considerable overlap between patients with CPP and other benign causes (17). Additionally, the diagnostic thresholds for uterine and ovarian volumes may vary (26). The reasons for these differences in cutoffs may include ethnic disparities, differences in body size, inter-radiologist variations, and disparities in performance among ultrasonography machines (28). Despite the absence of precise and standardized dimensional cutoffs, pelvic ultrasonography is an efficient tool for differentiating CPP from premature thelarche (PT) (31), especially when the results of the GnRH stimulation test are equivocal (28). Generally, the presence of a midline endometrial echo, uterine length > 4 cm, transverse diameter higher than 1.5 cm or uterine volume higher than 2.0 mL in girls with premature breast development makes a diagnosis of precocious or early puberty highly likely (27).

The primary objective of our study was to evaluate the diagnostic accuracy of pelvic ultrasonography parameters in identifying CPP in a cohort of female children undergoing gonadotropin stimulation tests and to assess the association of various ultrasonography measurements with the LH peak observed during the GnRH test.

Patients and Methods

Study characteristics

We conducted a single-center, observational, retrospective study to investigate the diagnostic accuracy of pelvic ultrasonography in female children with suspected CPP who underwent GnRH testing for diagnostic confirmation. Ethics committee approval was not obtained because the General Authorization to Process Personal Data for Scientific Research Purposes (Authorization No. 9/2014) states that retrospective archival studies using ID codes that prevent the direct

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tracing of data to the patient do not require formal ethics approval (22). However, all parents of the recruited patients were informed about the purpose of this study and signed an informed written consent form authorizing access to the medical records of the children and the processing of personal data. Of all patients considered, none refused to participate in our study.

Patient selection

We collected and analyzed data from the electronic medical records of patients. After the first screening process, we preselected 47 patients who were regularly followed up at the Pediatric Endocrinology Unit of the Fondazione Policlinico Universitario A. Gemelli IRCCS between November 2019-November 2023. All patients in our study were evaluated for suspected CPP (age < 8 yr and clinical characteristics compatible with the onset of puberty) and underwent a comprehensive endocrinological follow-up. In our center, we have a dedicated pediatric ultrasonography service capable of studying newborns and patients under 1 yr of age, and one of the authors of our paper (G.M.) is responsible for all pelvic ultrasonographic examinations in pediatric patients. Therefore, the mean age of our patient cohort was 6.4 yr from a *minimun* age range of 0.9 to a *maximun* of 7.9 yr (median value 6.92 yr, interquartile range, 1.1). None of the patients was taking any medications that could influence the hypothalamic-pituitary axis. All pre-selected patients underwent a comprehensive endocrinological assessment, including at least two visits spaced 6 months apart, a standard GnRH test, and pelvic ultrasonography with measurements of uterine and ovarian diameters and volumes. The indication for prescribing the GnRH test was an enlargement of the mammary glands or the development of secondary sexual characteristics, together with an acceleration of growth speed found between two visits spaced 6 months apart. None of the patients refused to undergo this test. Pelvic ultrasonography was performed using a transabdominal approach with a conventional, full-bladder, 3.5-5 MHz convex transducer, and interpretations were conducted by a skilled and trained physician (G.M.). Transverse and longitudinal sections were utilized to visualize the uterus and ovaries, respectively.

Data extraction

The data (**Table 1**) were collected from an electronic database for subsequent statistical analyses. All patients included in this study underwent the GnRH test, with gonadotropin levels measured following stimulation with GnRH at a dosage of 2.5 mcg per kg of body weight intravenously. The parameters recorded included the basal levels of LH and FSH as well as their values at 30, 60, and 90 min after GnRH stimulation. Additionally, we collected information on the auxological parameters of the girls and their family medical histories.

Ultrasonographic data collected systematically included:

- Uterine length
- Anterior-posterior diameter of the uterus
- Ratio between the fundus and cervix portions of the uterus
- Presence of endometrial echoes
- Uterine volume (longitudinal diameter × anteroposterior diameter × transverse diameter × 0.5233 mm).
- Ovarian volume (longitudinal diameter × anteroposterior diameter × transverse diameter × 0.5233 mm).
- Presence of ovarian follicles.

Table 1. Auxological, laboratory and ultrasonographic characteristics of our patient cohort with suspicion of central precocious puberty (CPP)

	Number of patients Total: 47 (n CCP; n Non-CPP)	Total Mean ± SD (Max–Min)	CPP Mean ± SD (Max–Min)	Non-CPP Mean ± SD (Max–Min)
Age (yr)	47 (34; 13)	6.40 ± 1.7 (7.9–0.9)	6.31 ± 1.97 (7.9–0.9)	6.64 ± 0.74 (7.5–4.7)
Basal FSH (IU/L)	47 (34; 13)	4.55 ± 3.31 (14.1–0.6)	5.20 ± 3.59 (14.1–0.6)	2.85 ± 1.47 (5.6–0.7)
Basal LH (IU/L)	47 (34; 13)	1.09 ± 1.44 (5.3–0.1)	1.41 ± 1.55 (5.3–0.1)	0.26 ± 0.55 (2.1–0.1)
Basal LH/FSH ratio	47 (34; 13)	0.25 ± 0.30 (1.24–0.01)	0.29 ± 0.28 (0.99–0.01)	0.14 ± 0.32 (1.24–0.02)
Endometrial thickness (mm)	27 (25; 2)	1.22 ± 0.35 (2.4–1.0)	1.24 ± 0.36 (2.4–1.0)	1.0 ± 0 (1.0–1.0)
FSH peak (IU/L)	47 (34; 13)	16.76 ± 11.87 (62.4–2.9)	19.24 ± 12.88 (62.4–7.6)	10.26 ± 14.55 (16.6–2.9)
Peak FSH sample (min)	47 (34; 13)	53.62 ± 20.68 (90–30)	52.06 ± 21.28 (90–30)	57.69 ± 19.21 (90–30)
Left ovarian volume (mL)	47 (34; 13)	1.87 ± 1.30 (8.2–0.3)	1.71 ± 0.84 (3.4–0.3)▲	2.28 ± 2.08 (8.2–0.5) ◊
LH peak (IU/L)	47 (34; 13)	12.63 ± 12.88 (54.5–0.8)	16.64 ± 13.11 (54.5–5.3)	2.27 ± 1.14 (4.6–0.8)
Peak LH sample (min)	47 (34; 13)	38.30 ± 17.36 (90–30)	40.59 ± 19.37 (90–30)	32.31 ± 8.32 (60–30)
Peak LH/FSH ratio	47 (34; 13)	0.82 ± 0.66 (3.1–0.1)	1.03 ± 0.5 (3.1–0.1)	0.26 ± 0.22 (0.9–0.1)
Right ovarian volume (mL)	47 (34; 13)	1.82 ± 1.15 (6.7–0.4)	1.73 ± 0.83 (3.6–0.4) ▲	2.06 ± 1.75 (6.7–0.4) ◊
TSH (microIU/mL)	47 (34; 13)	2.97 ± 1.18 (5.70–1.15)	3.20 ± 1.19 (5.70–1.24)	2.39 ± 0.97 (4.65–1.15)
Uterine volume (mL)	46 (34; 12)	2.14 ± 1.27 (8.0–0.8)	2.09 ± 0.99 (6.0–0.8)	2.28 ± 1.90 (8.0–1.1)

▲ Mean = 1.8, ◊ Mean = 1.4.

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Data interpretation

The circulating LH value used as a cutoff for CPP diagnosis may vary depending on the laboratory methods employed (23). However, in 2009, the joint Consensus Statement of the European Society for Pediatric Endocrinology and the Lawson Wilkins Pediatric Endocrine Society suggested that LH levels ranging between 3.3 and 5.0 IU/L after 30–40 min following the administration of GnRH are indicative of CPP (24). At our center, we consider a stimulated LH value > 5 IU/L as a 'diagnostic' criterion for CPP, in accordance with national guidelines (2).

Regarding pelvic ultrasonography findings, we deemed the following observations indicative of pubertal activation (2):

- Uterine length ≥ 3.6 cm
- Uterine antero-posterior diameter > 1 cm
- Uterine ratio (fundus/cervix) > 1
- Uterine volume > +2 SDS (25)
- Endometrial thickness > 5 mm (17, 25, 26)
- Ovarian volume > = 2 mL
- Right/Left ovarian volume > +2 SDS (25)
- Presence of at least one ovarian follicle > 5 mm (18, 29)

The interpretation of pelvic ultrasonogrphy results to identify pubertal activation requires the assessment of at least one of the following features:

- Presence of one pubertal uterine parameter (Uterine length ≥ 3.6 cm and/or Uterine antero-posterior diameter > 1 cm and/or Uterine ratio (fundus/cervix) > 1 and/or Uterine volume > +2 SDS and/or Endometrial thickness > 5 mm).
- Presence of one pubertal ovarian parameter (Ovarian volume > = 2 mL and/or Right/Left ovarian volume > +2 SDS and/or presence of at least one ovarian follicle > 5 mm).

We used the pubertal ovarian parameter feature based on the findings of Yuan *et al.* (29), who demonstrated that the number of follicles measuring 4 mm or more was significantly higher in the CPP group. Eksioglu *et al.* (18) also showed that multicystic ovaries with more than five follicles measuring less than 10 mm could indicate any form of precocious puberty in children aged 0–8 yr old.

Statistical analysis

Categorical variables are expressed as numbers, and continuous variables are expressed as means and standard deviations. For continuous variables, the Shapiro-Wilk test was used to determine whether the distribution was normal. The Spearman correlation test was conducted to determine the correlation between the ultrasonographic and laboratory parameters because not all continuous variables showed a normal distribution. In addition, the Mann-Whitney U test was conducted to determine whether there were significant differences in laboratory variables between patients with pubertal and non-pubertal pelvic ultrasonographic features. Statistical analyses were performed using IBM SPSS statistics software (version 25.0; IBM Corporation, Armonk, NY, USA). In all cases, statistical significance was set at alpha < 0.05.

Results

We retrospectively analyzed the clinical data of 47 girls with suspected CPP who underwent GnRH testing. Thirty-four of the 47 patients (72.34%) had a subsequent diagnosis of CPP based on the current laboratory diagnostic criteria (LH peak > 5 IU/L). Based on the previously reported ultrasonographic interpretation criteria, we observed that 39 out of 47 children (82.97%) included in this study displayed pubertal features in their pelvic ultrasonography results. Among the children included in the CPP group, 31 out of 34 children (91.17%) displayed pubertal features in their pelvic ultrasonography results.

In 13 out of 47 girls (27.65%), a CPP diagnosis was ruled out because the peak LH value detected during the stimulation test was lower than our diagnostic cutoff value. In these 13 girls in whom the GnRH test showed a pre-pubertal response, the final diagnosis was "early idiopathic thelarche." Among these 13 patients, eight exhibited pubertal ultrasonographic features, despite the pre-pubertal GnRH test results. Five of the 47 girls (10.6%) had a prepubertal peak LH value, and pelvic ultrasonography findings were not indicative of pubertal activation. We found a concordance between the results of the GnRH test, indicative of pubertal activation, and the presence of pubertal pelvic ultrasonography features detected in 31 out of 34 children (91.17%). According to these data for our patient cohort, pelvic ultrasonography findings had a sensitivity of 91.17%, a specificity of 38.46%, and a diagnostic accuracy of 31.10% for differentiating CPP from premature thelarche and other causes of normal pubertal development. Regarding individual ultrasonography parameters, the sensitivity, specificity and diagnostic accuracy values for uterine volume > 2 SD were 73.52%, 58.33%, and 69.56%, respectively; for uterine length ≥ 3.6 cm were 61.76%, 81.81%, 66.7%, respectively; for uterine antero-posterior diameter > 1 cm were 73.52%, 81.81%, 75.55%, respectively; for right ovarian volume were 70.58%, 61.53%, 68%, respectively; for left ovarian volume were 70.58%, 53.84%, 65.95%, respectively; for ovarian volume > = 2 mL were 64.70%, 53.84%, 61.70%, respectively; and for the presence of at least one ovarian follicle > 5 mm were 58.82%, 69.23%, 61.70%, respectively. A uterine ratio (fundus/cervix) of >1 was not analyzed because it was not available for the majority of our patients.

Correlation analysis

We conducted a correlation analysis between ultrasonographic parameters and laboratory test results, particularly for basal gonadotropin levels and their

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concentrations after GnRH stimulation. A statistically significant correlation was found between the right ovarian volume and basal LH levels (rho = 0.304; p = 0.038) and between the right ovarian volume and basal LH/FSH ratio (rho = 0.401; p = 0.005). A statistically significant correlation was also found between the left ovarian volume and basal LH levels (rho = 0.346; p = 0.017) and between the left ovarian volume and basal LH/FSH ratio (rho = 0.414; p = 0.004). These findings confirm that ultrasonographic parameters correlate with the results of the GnRH stimulation test and could anticipate diagnosis of CPP.

Further, we conducted a correlation analysis among various laboratory parameters, demonstrating a statistically significant correlation between the LH peak and basal LH levels (rho = 0.679; $p < 0.001$) and between the LH peak and basal LH/FSH ratio (rho = 0.518; $p < 0.001$). Therefore, basal gonadotropin levels should also be considered in the diagnostic suspicion of CPP, since they could anticipate a definitive CPP diagnosis in selected cases.

Mann-Whitney U test

The Mann-Whitney U test was conducted to determine whether laboratory variables were statistically different for patients with pubertal and non-pubertal pelvic ultrasonography features. A statistically significant difference was found for basal LH level, peak LH level, basal LH/FSH ratio, and peak LH/FSH ratio, with higher values in the group with pubertal pelvic ultrasonographic features (p = 0.026, p = 0.011, p = 0.031, p = 0.004, respectively) (**Fig. 1**).

Discussion

The diagnosis of CPP remains a complex process, as it necessitates a multidisciplinary assessment of patients with integration of historical, laboratory, and radiological data (2). Conventionally, the results of the GnRH test allow a confirmation or exclusion of pubertal activation.

In this study, we conducted a retrospective single-center analysis to assess the diagnostic reliability of transabdominal pelvic ultrasonography for confirming CPP. In our cohort of girls with suspected CPP, ultrasonography findings were able to anticipate a CPP diagnosis in 91.17% of cases, showing a sensitivity of 91.17% and a specificity of 38.46%. In some cases, pelvic signs of pubertal activation can differentiate rapidly progressive precocious puberty from other forms: Calcaterra *et al.* showed that a longitudinal uterine diameter ≥ 3.5 cm, transverse uterine diameter ≥ 1.5 cm, presence of an endometrial echo, and an ovarian volume ≥ 2 mL were associated with rapid and progressive pubertal development (32).

The action of gonadotropins increases the volume of the female gynecological apparatus, and ovarian and uterine activations usually occur simultaneously. Therefore, it is unclear whether ovarian or uterine dimensional increase is more significant for diagnosis. Yuan *et al.* conducted an observational study comprising 669 girls with Tanner breast development stage II, subsequently divided them into a CPP group (n = 350) and a PT group (n = 319), and conducted rectal ultrasonography to evaluate the pelvis in all patients. They studied the longitudinal, transverse, and anteroposterior diameters of the uterus and found that the uterine volume was significantly larger in the CPP group than in the PT group (29). Lee *et al.* conducted a similar analysis, recruiting 192 patients (n = 93, 48.4% with confirmed CPP), and demonstrated a significant increase in uterine volume when the hypothalamic-pituitary-gonadal axis was activated (30).

In contrast to the above studies, where uterine parameters responded to hormonal changes, our data revealed a positive correlation between ovarian volume and basal LH and between ovarian volume and the basal LH/FSH ratio. Based on these results, we hypothesized that the hormonal activation characteristics of girls with CPP may induce changes in the ovarian diameter and volume earlier than similar alterations of uterine

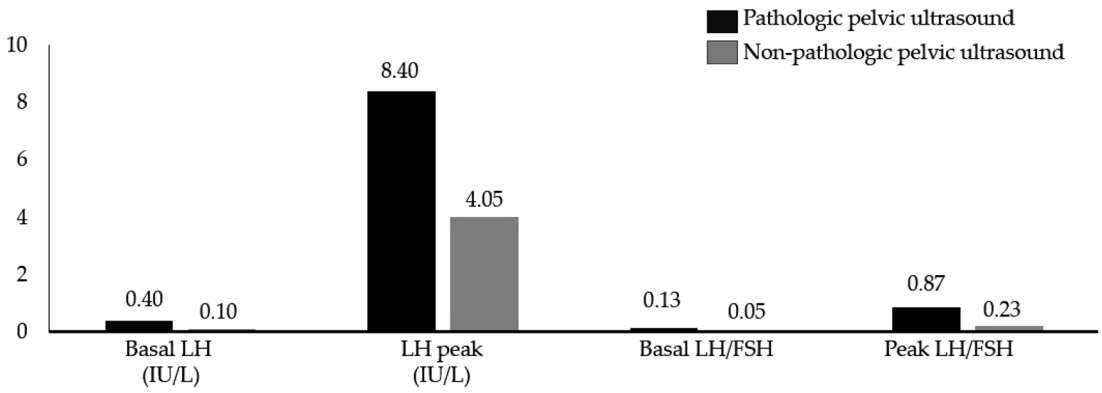

Fig. 1. Differences in the median values for basal LH, LH peak, basal LH/FSH ratio and peak LH/FSH ratio between the groups of patients with "pathologic" and and "non-pathologic" pelvic ultrasonography findings.

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diameter and volume. Indeed, Herter *et al*. demonstrated that a mean ovarian volume higher than 1.0 mL had 100% sensitivity and specificity for discriminating between prepubertal girls and girls with CPP (20).

In our study population, 32 out of 37 patients with CPP exhibited pubertal pelvic ultrasonographic findings, while 5 out of 37 patients displayed normal pelvic ultrasonographic features, with prepubertal ovaries and uterus. This finding may be explained by the Mann-Whitney U test conducted to determine whether laboratory variables differed statistically between patients with pubertal and non-pubertal pelvic ultrasonographic features. A statistically significant difference was found for basal LH level, peak LH level, basal LH/FSH ratio, and peak LH/FSH ratio, with higher values in the group with pubertal pelvic ultrasonographic features. Moreover, changes in the ovaries and uterus occurred slowly. It is possible that because of an early diagnosis of CPP in these five patients, more time needed to elapse before changes in the volume of the uterus and ovaries induced by gonadotropins materialized. To date, a multidimensional patient evaluation based on symptoms, clinical signs, and results from noninvasive baseline laboratory or radiographic tests has allowed for the diagnosis of numerous endocrinopathies (33). An early diagnosis of CPP is crucial for preventing the long-term complications of early pubertal development (34). Therefore, pelvic ultrasonography can be considered a rapid, easily reproducible, and cost-effective method that can complement the results of the GnRH test and, in most cases, anticipate the diagnosis of CPP without resorting to invasive tests (2).

In patients with CPP, the administration of GnRH analogs stops the progression of secondary sexual characteristics and can induce a decrease in the size and volume of ovaries and the uterus. de Vries *et al*. demonstrated that during the first 6 months of therapy with GnRH analogs, all 31 girls with CPP showed a significant decrease in the size of at least one of the uterine or ovarian parameters (35). Ambrosino *et al*. confirmed that the ovarian volume decreased more rapidly than the uterine volume during CPP therapy, highlighting the positive correlation between gonadotropins and pubertal development (36).

Conversely, in our study, we found that in 10 patients with PT, 7 out of 10 displayed pubertal pelvic ultrasonography features, as also shown by Eksioglu *et al*. who demonstrated that the ovarian volume in the PT group was similar to that in the CPP group (18).

The present study has some limitations, as it is a single-centre retrospective study, and because the sample size is limited. We did not perform any analysis for subgroups to differentiate the girls by ethnicity, and our findings may not be applicable to the general population. Nonetheless, we have highlighted the importance of pelvic ultrasonography in the diagnosis of CPP and its high concordance with results of the GnRH test. Future studies conducted on larger samples of patients may confirm these results and allow for a diagnosis of CPP without performing hormonal stimulation tests.

Conclusion

In our pediatric cohort with CPP, pelvic ultrasonography displayed a sensitivity of 91.17% and a specificity of 38.46% and was able to differentiate CPP from premature thelarche and other causes of normal pubertal development. Despite these findings of the present report, the GnRH test remains the gold standard for diagnosing CPP currently, even though it is an invasive method that requires the consent of the child patient and involves venous access and serial blood sampling for GnRH analysis.

Our present data also highlight a positive correlation between circulating levels of basal LH, LH peak, basal LH/FSH ratio, peak LH/FSH ratio, and pubertal pelvic ultrasonography findings. A diagnosis of CPP in girls still requires a multidisciplinary evaluation, although increased ovarian or uterine volume may be significantly correlated with the results of the GnRH test.

The possibility of diagnosing CPP through a non-invasive, cost-effective, and easily executable method, such as pelvic ultrasonography, remains one of the diagnostic challenges of the coming years.

Conflicts of interests: The authors declare no conflicts of interest.

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