

## Precocious puberty and COVID-19 in Argentina

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Historically, the age of menarche has been decreasing worldwide,<sup>1</sup> although it was believed to have stabilized in recent decades, despite an earlier onset of thelarche, which resulted in longer puberty.<sup>2</sup> However, according to reports from the past 5 years, there has been an increase in consultations for central precocious puberty, which further intensified during the lockdown due to the COVID-19 pandemic.

In girls, precocious puberty (PP) is defined as pubertal onset before 8 years of age. More than 90% of PP cases in girls is central (gonadotropin-dependent) and the vast majority is idiopathic or familial, not due to an organic cause.<sup>3</sup> When the onset of puberty in girls occurs between 8 and 9 years of age, it is considered early and, in the face of a rapid progression, the recommendation is to treat it like PP. Rapidly progressive early puberty (RPEP) is defined as the change from one Tanner stage to another in less than 6 months. As the vast majority of PP cases occur in girls and the increase in cases during the pandemic was also observed mainly in girls, there are no references to PP in boys in this comment or in the articles mentioned in this comment.

There are no local data available on the incidence of PP, but an incidence of 9 new cases per 100 000 girls has been described in other

populations (Denmark). Due to the striking and, in theory, subjective increase in PP consultations during the pandemic, more articles have been published in recent years. The first report on such epidemiological change was made in Italy, where S. Stagi<sup>4</sup> described an increase in the incidence of new cases of PP and accelerated pubertal progression during the COVID-19 lockdown, compared to figures from the same facility during the previous 5 years, and found that the group with PP during the pandemic was associated with a higher body mass index (BMI) and more hours of exposure to electronic screens. Also in Italy, during 2022, a 5-center retrospective study was published, which observed an increase of more than 100% in consultations for suspected PP in 2020 compared to 2019, with a higher prevalence of PP diagnosis in 2020. That multicenter study did not observe an increase in BMI in the group of girls with PP diagnosed during the pandemic, but did find a significant change in BMI between birth and PP diagnosis among girls diagnosed with PP during both 2019 and 2020.<sup>5</sup> During the pandemic lockdown, changes in eating habits, increased screen time, a sedentary behavior, stress, and sleep-wake cycle alterations were observed, all possible causes of earlier puberty in some girls. In recent years, advances have also been made

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in the identification of the genetic causes of PP, some associated with metabolic alterations, overweight, and hyperinsulinism.<sup>6</sup>

Recently, in Argentina, 2 independent groups published studies on this subject, and a national survey was conducted among pediatric endocrinologists on the perception of the increase in PP cases during the pandemic.

The study by Benedetto et al. described the incidence of PP in girls between 2010 and 2021. It found a stable annual incidence between 2010 and 2017 (average annual percent change of 0.2%) and a significant increase from 2017 onwards (average annual percent increase of 59.9%). When PP cases occurring during the pandemic were assessed specifically, an association was established with age at maternal menarche and a family history of PP. They found no differences in BMI, exposure to exogenous agents, physical activity, screen use, sleep hours, or changes in family climate between PP cases during the pandemic and controls.<sup>7</sup>

Geniuk et al. conducted an observational, retrospective study comparing 3 periods, 2 before the pandemic (April 2018–March 2019 and April 2019–March 2020) and 1 during the pandemic (April 2020–March 2021). Of the total number of consultations at the Department of Pediatric Endocrinology in their hospital, consultations for suspected PP doubled during the pandemic, from 10–11% in the pre-pandemic periods to 21.7% in the pandemic period. A higher frequency of female patients (95%) was observed in consultations for suspected PP across the 3 periods.

They also did not find an increase in BMI in the group of PP during the pandemic, and the only differences were that the girls in the pandemic period showed a higher percentage of RPEP and that in their initial physical examination they had more advanced breast development (Tanner stage) and larger uterine size (ultrasound).<sup>8</sup>

Arcari et al. conducted a survey among Argentine pediatric endocrinologists in December 2021. The survey results confirm the increase in consultations for PP during the pandemic, with more patients accessing treatment, either for PP or RPEP, in agreement with data published in other regions.<sup>9</sup>

Based on the studies mentioned above, it is clear that during the COVID-19 pandemic there was a marked increase in cases of PP and RPEP in the female sex, requiring treatment in the majority of cases worldwide. Although there is

no clear association between a higher BMI and PP (some initial studies associated them, but subsequent studies could not confirm it), I believe that there are many components of the pandemic lockdown (such as a sedentary behavior, stress, sleep-wake cycle alterations, and electronic screen exposure) that may have contributed to varying extents. Some reports highlighted a family history of PP, which is surely a basis on which, in some cases, the other factors acted to trigger an early pubertal onset or RPEP.

The increased incidence of PP was also noticed by pediatricians, who became familiar with the diagnosis, treatment, and consequences of untreated PP (final short stature and psychoemotional disorders in some cases) and timely referred patients for assessment and management.

The pandemic was a worldwide challenge, not only for some medical specialties in particular (infectious diseases, pulmonology, emergency departments), but also for other fields of medicine that are not directly related to the virus, but that were affected by the changes in habits suffered by the population, in this case, the girls who developed PP or RPEP.

Despite all the evidence mentioned above, a local multicenter study is required to assess the current incidence and clinical characteristics of PP in the Argentine population. ■

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