



## EDITORIAL

### Body mass index, tri-ponderal mass index, and pubertal growth pattern: New data in a Spanish population<sup>☆</sup>



### Índice de masa corporal, índice de masa triponderal y patrón de crecimiento puberal. Nuevos datos en población española

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Growth and puberty are two of the most fascinating phenomena of human physiology. Abnormalities in these processes are a frequent reason for seeking paediatric care and are therefore highly relevant in clinical practice. However, their diagnosis may pose significant challenges due to their complexity and our limited knowledge on the subject.

On the other hand, certain parameters, such as the height and body mass index (BMI), are highly relevant, since they are used as biomedical indicators of wellbeing in specific populations.

In Spain, there has been a growing interest in recent years in learning more about these biological indicators, as evinced by the numerous cross-sectional and longitudinal studies conducted by different research groups that now serve as reference standards.

We are aware of a secular trend towards faster growth and earlier puberty that has become more pronounced in recent years. While prepubertal growth is similar in individuals of either sex, during puberty there are different growth patterns that culminate in the same final heights. Therefore, using a single reference standard for the entire population in this stage of development may lead to significant errors

in diagnosis and therefore to the prescription of treatments that may not be justified in many cases.

The BMI and its normal ranges have gained importance in recent years due to the increasing prevalence of obesity in the paediatric population. This is the variable that has been used in everyday clinical practice to assess the degree of obesity due to its easy calculation, and it is the standard parameter currently used in all consensus documents. However, its association with visceral fat and thus with the risk of metabolic syndrome is in question, especially during puberty, a stage characterised by very rapid growth.

The cross-sectional study published by Carrascosa et al.<sup>1</sup> on growth patterns took as reference the entire paediatric population and did not differentiate subjects based on the degree of excess weight. In their most recent study, the authors focused on a healthy non-obese population studied at a later time period and stratified by age at pubertal growth spurt onset into five different groups, as had been done in previous studies, but with a larger number of participants per group. This study included 1,453 healthy children of both sexes with weights in the normal range and analysed changes in BMI and also in a novel parameter, the triponderal mass index.<sup>2</sup> This parameter was originally proposed in a recent publication because it may provide a more accurate estimate of the percent body fat, but it has been described in only one study, and so further research is required to corroborate its results.<sup>3</sup>

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This longitudinal study did not find differences in BMI between sexes.

The results were similar to those of other longitudinal studies conducted in Spain since 1988, although the BMI values were lower compared to previous cross-sectional studies. When it came to the prevalence of malnutrition, the findings were similar to those of studies published in other countries, but this was not the case when it came to obesity, which can probably be attributed to differences in methodology and the populations under study.

On the other hand, the onset of puberty is one of the clearest and most sensitive milestones that reflect the changes that occur in the evolution of the species. We know that puberty starts from age 8 years in girls and age 9 years in boys.

The onset of puberty is determined in part by genetic factors involved in the activation and inhibition of the secretion of gonadotropin-releasing hormone by the hypothalamus, the genes in the kisspeptin/kisspeptin receptor system and the gene that encodes the MKRN3 protein (makorin ring finger protein 3), as well as other genes such as DLK1 (Delta Like Non-Canonical Notch Ligand 1) or KCNK9 (potassium channel subfamily K, member 9), all of which have been recently described in association with patients with precocious puberty.

On the other hand, the onset of puberty is also strongly influenced by the exposome, which comprises all the general or individual environmental factors that may be involved in epigenetic changes, such as toxins, nutrition, physical activity, etc. The exposome, for instance, can explain the presence of a north-south gradient in the onset of puberty in Europe, with earlier onset in the Mediterranean region, and also the earlier age at onset of puberty of adopted or immigrant girls, among other phenomena.

We know that there has been a downward secular trend in the age of menarche in the last 200 years. However, recent studies have demonstrated that while the decline in the age at the onset of puberty has been more pronounced in girls, the age of menarche has remained stable.<sup>4</sup> On the other hand, psychological maturation is not evolving in synchrony with pubertal development, as used to be the case, which poses significant challenges in everyday clinical practice.

For this reason, the classification into five pubertal maturity groups based on the onset of puberty is a better fit for everyday clinical practice, as it helps get a clearer perspective of the development of each patient.

In their latest study with a larger sample, Carrascosa et al. aim to make it even clearer that this window in human development that is puberty varies significantly between individuals.<sup>5</sup>

At approximately age 5–6 years, the adipose rebound occurs in both sexes, and differences in weight, height and height velocity start to occur between sexes and maturation groups. In a longitudinal study, Aksglaede et al.<sup>6</sup> described an inverse correlation between BMI at age 7 years and age at the onset of the pubertal growth spurt, and found no association between this and the increased prevalence of obesity in the general population. However, this does not seem to always be the case, as in clinical practice we come across girls of this age with normal weight that consult due to early

breast development, which may or not be associated with the presence of signs of pubertal maturation of the internal sex organs on ultrasound.

In all groups, the onset of the pubertal growth spurt occurred when the BMI reached a value of approximately 17.8 kg/m<sup>2</sup>, but this took place at a different age in each group. Individuals that had earlier onset grew more and for a longer time, as had been described by other authors.<sup>3</sup> This would support the "critical weight hypothesis", according to which BMI would be associated with the onset of puberty, so that leptin, a hormone produced in adipose tissue, would inform the hypothalamus that the timing is right to trigger this event, and the hypothalamus in turn would activate the hypothalamic-pituitary-gonadal axis through the KISS1/KISS1R system.

Therefore, it does not seem that there is one easily identifiable factor that can define the onset of puberty in the general population. There may be one such factor in the most extreme cases. Whatever it may be, new information contributed by scientific fields such as transcriptomics, proteomics and metabolomics will presumably help us gain a more thorough understanding of the processes that take place in the prepubertal period up to age 7 years, so that we can compare them to those that occur in subsequent years, which would allow us to better define the key factors at play in the physiological phenomenon that is puberty.

To conclude, it is fair to say that the studies published by Carrascosa et al. are extremely relevant to the everyday practice of paediatrics, as they provide current data on BMI values in the non-obese population and the patterns of pubertal growth. Their findings clearly demonstrate that there are differences in the timing of onset of puberty between individuals that fall within the normal range. Those that have earlier onset grow more and for a longer time, with all reaching the same final height.

## References

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