Obesity and Growth during Childhood and Puberty

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Abstract

Growth during childhood and adolescence occurs at different rates and is influenced by the interaction between genetic and environmental factors. Nutritional status plays an important role in regulating growth, and excess body weight early in life can influence growth patterns. Childhood obesity is a growing and alarming problem, associated with several short-term and long-term metabolic and cardiovascular complications. In addition, there is evidence suggesting that excess adiposity during childhood influences growth patterns and pubertal development. Several studies have shown that during prepubertal years obese children have higher height velocity and accelerated bone age compared to lean subjects. However, this prepubertal advantage in growth tends to gradually decrease during puberty, when obese children show a reduced growth spurt compared with lean subjects. Growth hormone (GH) secretion in obese children is reduced, therefore suggesting that increased growth is GH independent. Factors which have been implicated in the accelerated growth in obese children include increased leptin and insulin levels, adrenal androgens, insulin-like growth factor (IGF)-1, IGF-binding protein-1 and GH-binding proteins. Excess body weight during childhood can also influence pubertal development, through an effect on timing of pubertal onset and levels of pubertal hormonal levels. There is clear evidence indicating that obesity leads to early appearance of pubertal signs in girls. In addition, obese girls are also at increased risk of hyperandrogenism. In boys, excess adiposity has been associated with advanced puberty in some studies, whereas others have reported a delay in pubertal onset. The existing evidence on the association between childhood and adolescence obesity underlines a further reason for fighting the epidemics of childhood obesity; that is preventing abnormal growth and pubertal patterns.

Growth during childhood and adolescence occurs at different rates and is influenced by several factors including genes, hormones and nutrition [1]. In particular, hormones are key growth regulators, with a main role for the growth hormone (GH) insulin-like growth factor (IGF) axis, glucocorticoids, thyroid hormones and sex steroids [1, 2]. Several lines of evidence also support the important role of nutritional
status in regulating childhood growth [3]. Whereas poor nutrition is a well-known determinant of poor somatic growth and delayed pubertal onset and progression, excess body weight is associated with taller stature during childhood and with early pubertal development [4, 5]. In addition, childhood obesity has also been associated with endocrine abnormalities, such exaggerated adrenarche, hyperandrogenism as well as an increased risk of polycystic ovary syndrome [4].

Childhood obesity is a growing and alarming problem, and it represents an important determinant of morbidity [6]. The World Health Organization defines childhood obesity as one of the most serious public health challenges of the 21st century, due to its increasing prevalence at an alarming rate. Obesity is associated with several short-term and long-term metabolic and cardiovascular complications, which negatively influence the prognosis of young people [7]. There is also extensive evidence suggesting that excess adiposity during childhood may influence somatic growth and pubertal development [5, 8, 9]. The relationship between obesity and growth is two-ways: on the one hand rapid growth during infancy and early life can be a risk factor for later obesity; on the hand the development of excess adiposity early in life can affect growth patterns, by promoting accelerated growth and pubertal development and progression. This second aspect of the relationship between obesity and growth will be reviewed in this chapter.

**Growth Consequences of Childhood Obesity**

Several cross-sectional studies have shown that obese children tend to be taller and to present an acceleration of pubertal and skeletal maturation compared to normal weight youth [10, 11]. Longitudinal studies have allowed a better characterization of growth patterns in obese children and adolescents [8, 9]. Specifically, they have shown that during prepubertal years obese children have higher height velocity and accelerated bone age compared to their lean peers. However, this prepubertal advantage in growth tends to gradually decrease during puberty, when obese children show a reduced growth spurt compared with lean subjects. This latter effect together with the early pubertal maturation reported in obese children determines similar final heights between obese and nonobese children [8, 9].

A large Swedish study based on repeated height and weight measurements obtained from 319 girls and 304 boys showed that an increase in BMI between the ages of 2 and 8 years was associated with a parallel gain in height during the same time period [8]. In particular, for every 1 unit increase in BMI there was a 0.23 cm increase in height in boys and a 0.29 cm increase in girls. However, height gain during puberty was reduced in obese children and puberty started earlier. A gain of 1 unit of BMI between the age of 2 and 8 years was associated with a peak height velocity occurring 0.11 years earlier, and a reduced pubertal height gain of 0.88 cm for boys and 0.51 cm for girls. These latter phenomena contributed to the lack
of association between childhood BMI and final height [8]. Similar findings for the association between height and BMI during childhood and adolescence were reported by Denzer et al. [9] in a longitudinal study, where anthropometric data were collected from 1,232 Caucasian children and adolescents with an age range between 6 and 18 years. In this study, mean height SDS in obese children was constantly positive compared to normal weight children from the age of 6–14 years, but thereafter height SDS turned negative, indicating progressive loss of the childhood and early pubertal height advantage. A similar pattern was detected in bone age, which was significantly advanced during childhood and early puberty, whereas in older subjects tended to be normal or even retarded [9].

The higher growth in obese children appears to be mainly GH independent, given that GH secretion in obese children is reduced [12]. Factors which have been implicated in the accelerated growth in obese children include increased leptin and insulin levels, adrenal androgens, insulin-like growth factor (IGF)-1, IGF-binding protein (IGFBP)-1 and GH-binding proteins (GHBP) [12].

Abnormalities in the GH-IGF-1 axis are common among obese children and adolescents [12, 13]. Several aspects of the GH secretory patterns are altered, with decreased GH half-life, frequency of secretory episodes and daily production rate. In addition, GH secretion is impaired in response to all traditional pharmacological stimuli acting at the hypothalamus [12, 13]. However, although GH secretion is reduced in obese children, their GH responsiveness appears to be increased compared to normal weight peers. IGF-1 responses have been reported to be up to 80% higher in obese prepubertal children than control children during IGF generation tests [14].

At the peripheral level, obese subjects show increased circulating levels of GHBP, IGF-1, IGFBP-1, IGFBP-2 and IGFBP-3 in the pre- and intrapubertal period, reduced levels of IGF-1, IGFBP-1, IGFBP-2 and IGFBP-3 in the postpubertal stage as well as reduced ghrelin secretion [13, 15].

Interestingly, the abnormalities in the GH-IGF axis associated with obesity are reversible, as shown by the significant positive effect of weight loss on several parameters of the axis. Of note, after a period of weight loss there was a significant increase in measures of GH secretion [15]. In addition, weight loss had a significant effect on GHBP, with decreased levels paralleling reductions in BMI and leptin levels [16].

With regard to GH-independent factors promoting growth, increased adipose tissue aromatization of androgens into estrogens is one of the main mechanisms regulating growth in the context of obesity [4]. In addition, increased insulin levels, as a consequence of obesity-related insulin resistance, can act on the IGF-1 receptor and stimulate growth [4]. Leptin appears to be a key factor mediating increased growth in the context of obesity [17]. Animal models have shown that leptin can act as a skeletal growth factor, able to stimulate both proliferation and differentiation of chondrocytes in the growth plate [18].
Excess body weight during childhood can also influence pubertal development, through an effect on timing of pubertal onset and levels of pubertal hormonal levels [4].

An association between excess adiposity and early pubertal onset has been reported across different studies assessing girls belonging to different ethnic groups [11, 19–24]. Although the majority of these studies have been cross-sectional and based on BMI as an index of adiposity, the results have been quite consistent in showing a causal relationship between a larger body size during childhood and an earlier onset of the larche and age at menarche, as well as early manifestations of other measures of pubertal onset.

Interestingly, not only childhood growth, but even infant growth can promote an early onset of puberty. For example, a rapid weight gain from 4 months to 1 year has been associated with earlier age at menarche independently of subsequent childhood growth patterns [25].

The relationship between childhood obesity and early puberty in girls could be explained by insulin resistance/hyperinsulinemia associated with obesity. In particular, increased insulin levels can stimulate sex steroid production by acting on the adrenal glands, liver, ovary and fat cells. Increased androgen levels can in turn promote pubertal development acting peripherally and/or centrally on the hypothalamic pituitary axis [4]. Another key factor explaining the association between obesity and puberty is leptin, which can exert direct effects on the gonadotropin secretion [5].

Whereas the majority of studies have reported an anticipation of age at pubertal onset in obese girls, for boys there are contrasting findings among different studies.

A longitudinal study in US boys has shown that a higher BMI during early and middle childhood is associated with a later onset of puberty [26]. Similar results emerged from a large cross-sectional study on 1,500 girls and 1,520 boys (aged 8–14 years) who participated in the Third National Health and Nutrition Examination Survey (1988–1994). Subjects were classified as ‘early maturers’ if their entered a pubertal Tanner stage earlier than the median age for that stage. Interestingly, whereas across all ethnic groups the prevalence of obesity was higher among ‘early maturer’ girls, in boys the opposite occurred with a significant higher percentage of obese boys among ‘late maturers’ [23].

However, there are some studies which have reported early puberty in obese boys. In a longitudinal study Lee et al. [26] reported that a higher BMI gain during childhood induced anticipation in the timing of puberty of 0.6 years in boys. Data from a large cohort of Danish boys showed a significant positive association between higher BMI and earlier age at voice break, used as a maker of puberty [27]. A more recent large study exploring the relationship between prepubertal BMI and pubertal onset, assessed by age at onset of pubertal growth spurt and at peak height velocity,
again in Danish boys, confirmed that the heavier boys were at age 7, the earlier they entered puberty [28].

These discordant findings in boys are party explained by differences in the ways of assessing puberty. A direct assessment of pubertal stage has been performed only in few studies, whereas others have used some surrogate markers of pubertal onset/progression. Therefore, further studies are required to clarify the relationship between obesity and puberty in boys.

Another important point to underline in both boys and girls is that although not all studies have showed an effect of prepubertal BMI in the initiation of pubertal growth spurt, obesity can affect the progression of pubertal development, resulting in earlier attainment of later pubertal stages [24].

**Pubertal Hormonal Levels in Obese Boys and Girls**

Obesity in boys and girls has also been associated with abnormal levels of adrenal and gonadal hormones. Levels of dehydroepiandrosterone sulphate (DHEAS) have been directly associated with body weight in 8-year-old children, where they could contribute to the association between early growth and adult disease risk, by enhancing insulin resistance and central fat deposition [29].

Obese peripubertal girls show significant hyperandrogenism, as indicated by increased levels of total testosterone and free testosterone and decreased levels of sex steroid-binding globulin (SHBG) compared with those who are lean [30–32]. Insulin and LH contribute to increased testosterone in obese peripubertal adolescents, although other factors associated with obesity may also mediate this association [31]. Obesity is associated with low overnight LH pulse frequency in prepubertal and early pubertal girls whereas by Tanner stages 3–5, LH frequency is abnormally elevated in obese girls, possibly reflecting the effects of hyperandrogenism and resembling findings of adult polycystic ovary syndrome [33]. Interestingly, weight loss has been associated with a significant decrease in testosterone concentrations in obese boys and girls [34].

Overall, these data suggest that childhood obesity can contribute to the appearance of endocrine disturbances during adolescence, and may also increase the risk of developing polycystic ovary syndrome later in life.

**Conclusions**

Rapid weight gain during infancy and early life can influence growth and pubertal development.

In particular, during prepubertal years obese children tend to be taller, but this advantage then disappears, due to the decreased pubertal spurt. Abnormalities in the GH-IGF-1 axis are common among obese children and adolescents.
Obesity during early life is a risk factor for an early onset of puberty, mainly in girls, and the consequences associated with it. In boys there are opposite findings, with obesity being associated with delayed puberty in some studies and with advanced puberty in others.

Overall, the existing evidence on the association between childhood/adolescent obesity and growth/puberty underlines a further reason for fighting the epidemics of obesity, which is preventing abnormal growth and pubertal patterns.

References


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