Influences of Childhood Obesity on Pubertal Development

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Abstract

The process of pubertal development is only partly understood but is thought to be influenced by many partially unknown factors. During the 20th century, there was a secular trend towards earlier pubertal development. Due to the rising epidemic of childhood obesity, the relationship between body composition in childhood and the tempo and timing of puberty needs to be better understood. Studies have shown that there is a clear relation between reaching a critical body weight and pubertal onset and course. Moreover, a rapid and early weight gain during infancy, and even during foetal life, is associated with an earlier onset of menarche, an earlier pubertal growth spurt, an earlier thelarche in girls, an earlier pubarche in both sexes and an earlier increase in testicular volume in boys. Furthermore, there is a clear correlation between increasing body mass index and earlier pubertal development in girls. In boys, controversial data exist. The majority of studies propose that puberty and voice break occur earlier in obese boys when compared with normal-weight peers, but interestingly, a few studies show the opposite finding. The earlier onset of puberty that occurs in obese individuals could be mediated by factors that are directly linked to adipose tissue or could be an indirect effect of genetic and/or environmental factors. This review presents the current evidence on this topic, highlighting inconsistencies and opportunities for future research.

Introduction

Overweight and obesity are defined by the World Health Organization as abnormal or excessive fat accumulation that may impair health. In 2011, more than 40 million children under the age of five were overweight. Overweight in childhood is defined as a body mass index (BMI) above the 85th percentile and lower than the 95th percentile, whereas obesity is defined as a BMI above the 95th percentile. Puberty is the process of physical change by which a child’s body matures into an adult body that
is capable of sexual reproduction to enable fertilisation. Puberty is initiated by hormonal signals from the brain to the gonads: the ovaries in a girl, and the testes in a boy. On average, girls begin puberty at ages 9–11, and boys begin puberty at ages 10–12; girls usually complete puberty by ages 15–17, while boys usually complete puberty by ages 16–17.

To induce pubertal development, children need to have reached a certain body weight or at least a particular amount of fat [1–3]. Being underweight due to a condition such as anorexia nervosa, chronic illness or malnutrition can lead to delayed puberty and later subfertility. From the 20th century onwards, there has been a downward trend towards an earlier age at menarche that was thought to be due to improvements in nutrition and overall quality of life. This trend has now stabilised in many countries [4–7], but some countries, including the USA [8], Greece [9], and Jamaica [10], still report an advanced pubertal onset in their paediatric populations.

The increasing prevalence of obesity during childhood and adolescence is one of the major health problems in developed countries across Europe and in Canada and the USA, and this is a well-known statistic. However, obesity is also emerging as a significant problem in developing countries, where obesity and under-nutrition often co-exist [11]. The development of early comorbidities, including insulin resistance, dyslipidaemia, hypertension and other cardiovascular risk factors are often seen in overweight and obese youth, and metabolic syndrome is a diagnosis that is now often made on a regular basis in paediatric centres. Another complication, which is the major focus of this chapter, is the induction of earlier pubertal development in obese children [12–15]. Early puberty can lead to an imbalance in sexual and psychosocial maturation that can induce future health problems [16, 17]. Many previous studies have indicated a reasonably strong relationship between over-nutrition and the timing of puberty, giving rise to the critical mass theory [18]. This theory suggests that there is a critical fat mass (~17% body weight) required for menarche and a higher fat mass (22% body weight) needed to maintain reproductive capacity.

Given this relationship and the increasing prevalence of overweight and obese youths across the world, should we therefore expect a corresponding secular change in the timing of puberty [18]? At the moment, the data on this topic are controversial, and there is currently not enough evidence showing a direct association between global changes in obesity rates and early sexual maturation across the world. This article will therefore highlight and discuss the data that are available on this important but controversial topic. Due to the inconsistencies of the published data, it is necessary that we begin to plan new and interdisciplinary studies, ideally involving large numbers of youth who are followed over long periods of time, to better understand the trends in pubertal development. These types of studies also need to be linked to in vitro and in vivo investigations of the molecular mechanisms that govern puberty induction to find the missing links between adipose tissue and pubertal development [17, 19, 20].
Obesity

Childhood obesity is now a frequently seen condition, and its prevalence has only recently stabilised in many countries, including Germany [21]. However, the prevalence of childhood obesity is still much too high and even continues to rise in several countries around the world. Weight gain is the result of many different and diverse factors, such as exposure to an obesogenic environment and genetic traits that have evolved over time to facilitate fat storage [15, 22–25]. Children with lifestyle-induced obesity are often tall during childhood but have a normal final height, and this is often due to earlier (but still within the normal range) timing of pubertal development and hence earlier closure of the growth plates. Children who suffer from obesity due to specific genetic and/or hormonal conditions tend to be shorter than their predicted final height. These findings show that there are likely factors that affect both puberty and body composition [26–31].

Around 40–70% of the inter-individual differences in body weight can be explained by genetic variation – particularly in young children. Many different genes have been identified that impact body weight [32]. During evolution, different gene variants that guaranteed survival, even in times of malnutrition and starvation, have been selected. However, those conditions do not exist in our modern and obesogenic environment, and therefore, the selection of genes that promote overweight and obesity have become detrimental, leading to the development of weight-related metabolic complications [22, 33–35].

Furthermore, sociocultural surroundings can influence the development of obesity. For example, Christakis and Fowler have shown that an increase in body weight in one person can affect the body weight of friends, siblings, relatives and neighbours. Network phenomena, therefore, also seem to be relevant to the biological and behavioural traits of obesity, and obesity appears to spread through social ties [23, 36].

Pubertal Development

Puberty usually follows a typical pattern of development in both sexes. In girls, puberty usually starts at 9–14 years of age with breast development followed by pubic hair growth. In boys, true puberty starts at 10–15 years of age with an increase in testicular volume followed by pubic hair and enlargement of the penis. Pubertal development starts with activation of the hypothalamic-pituitary-gonadal axis. Changes in the production of the hypothalamic gonadotropin-releasing hormone (GnRH), the gonadotropins luteinising hormone (LH) and follicle-stimulating hormone and the sex steroids estradiol and testosterone lead to the manifestation of the first clinical signs of puberty. Pubic hair can develop independently from the activation of the hypothalamic-pituitary-gonadal axis (termed pubarche), for example, due to
androgen production in the adrenal glands [22]; this phase is termed adrenarche and does not represent true puberty. Clinically, pubertal status can be classified with the help of the Tanner stages (B1–5 for breast development, P1–6 for pubic hair development, and G1–5 for male genitalia development). Unfortunately, this method is biased by the subjective evaluation of the examination and can therefore lead to problems in clinical studies. However, one has to take into consideration that, in some cases, obese girls may have suffered from pseudo- or lipogynaecomastia instead of real thelarche. All pubertal changes usually occur over a period of 4–5 years. The beginning, duration and maturation of puberty are a result of a complex interplay between the central nervous system, endocrine glands and adipose tissue [37, 38]. Interestingly, the timing of puberty is often markedly different between different ethnicities [21], and there is also a large variation in the timing of puberty, which can vary by up to 4 years, in any given population.

An increase of the hypothalamic secretion of GnRH is an essential step for activating the pituitary-gonadal axis at the start of pubertal development. A short phase of GnRH system activation occurs during foetal development and during the neonatal period; however, reactivation in later childhood is thought to be critical for the induction of puberty, and sudden changes in GnRH secretion are the inductor, timer and supporter of pubertal maturation. The activation of the system underlies large inter-individual variations that reflect the complexity of puberty and indicate that puberty is not simply a function of chronological age. The mechanisms that impact the GnRH secretory network convey information about metabolic fuels, energy stores and somatic development. The primary activation of GnRH during the foetal and neonatal periods and the intensity of this initial activation might also affect the timing and onset of puberty [22, 37, 39].

Many definitions for the timing of puberty exist in the literature, and this can cause confusion when examining the impact of factors such as obesity on the timing and tempo of puberty. The definition of puberty can be based on the shape of the adolescent growth spurt, the timing of sexual characteristics, specific events like menarche in girls and voice break in boys or skeletal maturation [18]. All of these factors likely contribute to the reported large variation in the timing of the onset of normal puberty.

While pubertal timing appears to be largely influenced by genetics, as implied by studies in twins [26], Karlberg suggests in his review from 2002 that a single environmental factor stands out as most significant – possibly explaining as much as 25% of the variation in the timing of puberty. This factor, it is stated, is simply the nutritional status in childhood – over-nutrition and obesity seem to trigger pubertal onset. However, recent studies have identified that both shortness and thinness at birth are also associated with earlier pubertal maturation – the reverse of their impact during childhood years [18]. Longitudinal series as opposed to cross-sectional series should be used to characterise the various pubertal events in more detail, thus providing more trustworthy information.
Effects of Puberty on Childhood Obesity Development

More than 2000 girls were examined in the ‘National Health and Nutrition Examination Survey’. This survey consisted of a programme of studies that combined interviews and physical examinations to assess the health and nutritional status of adults and children in the USA. The mean age of menarche decreased by approximately 3 months in white girls and by 5.5 months in black girls in the USA between the late 1960s and approximately 1990, and this decrease was independent of weight. It is significant that the strongest evidence, i.e. the largest consistent changes, for the recent secular advancement of the onset and progression of puberty was found in the age at menarche for Mexican-American children and in black girls. These findings raise many questions concerning the definitions of race/ethnicity, concurrent secular changes in socioeconomic or health status, other USA minority populations, genetic potentials, and associations between changes in pubertal timing and obesity. In this study, the prevalence of early menarche was significantly increased if the girls had a BMI between the 85th and 95th percentile [17, 19]. Early pubertal development was also associated with a higher BMI and waist circumference in later life [40]. The studies in boys are less clear. One study investigated the effect of pubertal maturation and BMI on adipose tissue distribution and BMI during adulthood in 579 men [41, 42]. The age at the highest growth spurt correlated negatively with BMI, total body fat mass and central fat mass, but not with peripheral fat mass. An early start of pubertal development could therefore be a predictor for more centrally than peripherally increased fat mass in later life. A high amount of subcutaneous adipose tissue is rather a sign for a high BMI before puberty [42].

Obesity Influences Pubertal Development

Several studies on how childhood obesity can influence pubertal timing exist, but their results are sometimes controversial. The most important finding is that there are pronounced sex-dependent differences. A rapid weight gain during infancy (independent of birth weight) is associated with early pubertal development in both sexes. These data therefore support the hypothesis that fast body growth and rapid weight gain during infancy will influence pubertal development and induce earlier maturation [10].

Lue et al. found that a 1 unit (kg/m²) greater BMI value at 8 years of age is associated with approximately a 1.3- and 1.2-month earlier age at peak height velocity for boys and girls, respectively [43]. Furthermore, results of a German study on 1,421 pre pubertal children did not find significant differences in age when pubic hair was seen (of P2 Tanner) in lean and obese girls and boys. However, the age of thelarche was significantly earlier in obese girls, and an increase in testicular volume in boys appeared to be independent of BMI [44, 45].
In contrast, one study showed that childhood obesity could lead to a delayed timing of puberty. In 1,383 overweight and obese children, the following parameters were compared: body weight, height and timing of pubarche, menarche and voice break in a representative German childhood cohort aged 10–16 years [46]. Obese children were found to undergo later pubarche, menarche and voice break than their lean control group and hence presented with late puberty [46].

As described above, the study results are controversial. Therefore, it is of great importance to perform further and interdisciplinary studies to illuminate the connection between obesity and pubertal development and to better understand the sex-specific differences in these processes.

**Childhood Obesity and Pubertal Development in Boys**

Unfortunately, data about the connection between childhood obesity and pubertal development in boys is limited and controversial. Several studies have attempted to obtain significant and consistent data in relation to weight status and the timing and tempo of puberty [6, 22, 47–49].

One retrospective study included 1,520 men who were followed up until the age of 65. In this study, a high BMI during childhood was associated with an earlier timing of pubertal development [50], and children who showed late pubertal development were taller and leaner as adults. Furthermore, this study demonstrated that rapid weight gain during childhood resulted in early pubertal development and in shorter final height [50].

Another sign of pubertal maturation, the voice break, was evaluated in 436 choir-boys from Denmark. The age at voice break decreased from 14.0 to 13.7 years within 10 years [51], and there was a trend towards an earlier voice break with increasing BMI [17, 41, 51].

Another puberty study from Copenhagen investigated the secular trend of pubertal timing in boys over a period of 15 years [47], comparing the pubertal timing during years 1991–1993 to that in 2006–2008. The researchers found that puberty, defined as a testis volume of >3 ml, started earlier in 2006–2008. Furthermore, the LH levels in this group were significantly increased compared to that of the first group, and the BMI-Standard Deviation Score (BMI-SDS) was found to be significantly higher in the second set of investigations. Interestingly, there were no significant differences in pubertal timing and serum LH levels during the two time frames after adjusting the BMI-SDS. In conclusion, this study found earlier pubertal development that seemed to be associated with increasing BMI [47].

The current data and publications on this topic are controversial; however, both hypotheses appear to be valid in that childhood obesity in boys can lead to an earlier or even delayed puberty. However, the majority of studies has shown that childhood obesity tends to be linked with an earlier timing of pubertal development in...
boys, but there are still too many inconsistencies to be able to answer the question properly. Further well-planned and interdisciplinary studies are needed to clarify these data.

**Childhood Obesity and Pubertal Development in Girls**

A large number of diverse studies have evaluated the connection between childhood obesity and pubertal development in girls. The results in girls, more strongly than those in boys, support the hypothesis that childhood obesity will lead to an earlier puberty onset. The major problem with these data is that they are mostly derived from cross-sectional studies; therefore, questions about the causality of this early onset of puberty remain unanswered. Girls that have a high BMI-SDS (>1.88) have a high probability of menstruating earlier, and they present with an earlier pubertal development than lean girls [44, 52–54]. Early puberty in girls can be caused by overweight and obesity, and this is definitely more often the case than puberty leading to a massive increase in body weight [55, 56].

Whether the general decrease in age for pubertal onset is a result of the so-called ‘obesity epidemic’ remains to be fully elucidated. A Danish study measured the age at puberty, the start of the pubertal growth spurt and the highest growth velocity of 156,835 pre-pubertal children [57]. In this study, the BMI-SDS correlated negatively with the parameters of pubertal development and pubertal timing. However, a trend towards an earlier puberty that is independent of BMI has been proven in the last 39 years, perhaps suggesting that the obesity epidemic is not the only reason for the secular trend towards earlier puberty that was seen in the 1900s [47, 57, 58].

Children who are small at birth and who develop obesity during childhood are significantly younger at the age of menarche than same-aged, lean children. In addition, the effect of maternal obesity on the pubertal development of daughters has not been investigated in depth [59]; however, one publication has indicated that daughters of mothers who were obese during pregnancy menstruate earlier than daughters of lean mothers [60].

In Switzerland, a longitudinal study examined 650 girls aged 6–18 years and did not find any significant differences in the ages of pubarche of lean and obese girls [61]. However, there were significant differences in the timing of breast development. Tanner stage B3 was reached at 11.6 years in obese girls compared to 12.2 years in normal-weight girls, and dehydroepiandrosterone levels were elevated [61].

The study data on girls is consistent and quite clear. However, the criticism is that most of the studies just looked at the outcome and did not determine the causes and reasons for earlier pubertal timing and development. How much influence does growth behaviours have on pubertal maturation? This question was studied using the mother and child files of the ‘National Longitudinal Survey of Youth’ [62]. In this study, significant differences in BMI and height at the age of 6 years in different