The Importance of Knowing Growth and Pubertal Development in Down Syndrome

Giuseppe Cannalire*, Melissa Bellini and Giacomo Biasucci

Department of Paediatrics and Neonatology, Guglielmo da Saliceto Hospital, Cantone del Cristo, Piacenza, Italy

Abstract

Knowing growth and pubertal development in Down Syndrome (DS) is very important to early detect catch down growth/weight or pubertal delay that can be suggestive of disorders such as autoimmune diseases, endocrinopathies or oncological pathologies.

Keywords: Down syndrome; Growth; Pubertal development

Introduction

Knowing growth and pubertal development in Down Syndrome (DS) is very important to early detect catch down growth/weight or pubertal delay that can suggest disorders such as autoimmune diseases, endocrinopathies or oncological pathologies. These pathologies are more frequent in children with DS [1] and their presenting symptoms can be growth failure and delay of puberty because of poor food intake, increased caloric utilization and consequent abnormal neuroendocrine regulation of growth and puberty [2,3]. A prompt diagnosis and an appropriate therapy can reduce comorbidities and allow adequate catch-up growth/weight and pubertal development. Since growth in children with DS differs markedly from that of normal children, the use of DS specific growth charts is important for diagnosis.

Materials and Methods

We describe growth and pubertal development in children with DS using data in the medical literature.

Results

Compared to the general population, children with Down Syndrome (DS) show marked lower growth rates, growth failure being present since birth. Ultrasound can be used to detect intrauterine growth retardation at 15-16 week gestation. Studies reported the difference in birth weight between newborns with DS and their controls to range between 180 and 370 gr, with gestational age of 38 weeks versus 39.1 weeks [1,4]. Mean length at birth in children with trisomy 21 is reduced by about 0.5 Standard Deviation Score (SDS), as compared to their controls [5]. Head circumference, too, is reduced by about 1 SDS in newborns with DS compared to the control arm, the delay increasing up to 2 SDS in 5-6 month old infants [6].

Specific growth charts have been established for children with DS in different countries [6-12]. Published growth charts, in particular those proposed in the studies by Cronk et al. [12] demonstrated that growth delay in both length and weight in children with DS is more evident within the first two years of life. The reason why growth speed is more deficient in this period is still unknown [12]. Growth delay in nurslings with DS may be caused by insufficient nutrition due to feeding difficulties; hypotonia in newborns with DS may cause sucking problems, thus making breastfeeding difficult, especially when the presence of concomitant defects requires hospitalization [13].

Decreased growth rates are more evident during puberty, which has early onset in DS subjects and is generally anticipated as compared to healthy age-matched individuals, and it is associated with a decreased pubertal growth spurt [7,9].

Some studies have been carried out with the aim to verify whether impaired growth in DS patients is caused by altered growth hormone (GH) secretion. Some studies showed a normal GH secretion in DS patients, despite an altered neuroendocrine regulation with low levels of insulin-like growth factor-1 (IGF-1). In other studies IGF-1 and fetal serum levels of IGFBP were within normal ranges [14,15]. In another study, 72 prepubertal patients (44 out of 72 were males) with DS were treated with GH therapy showing growth improvement. At therapy beginning, patients showed levels of GH within lower limits (GH mean peak values of 8 mcg/l; range: 1.2-21.4). This finding seems to suggest that, contrary to other published data, impaired growth in prepubertal children with DS might be caused by GH deficiency. Further studies are needed to evaluate GH deficiency in DS and GH therapy side effects; in particular in the light of the acknowledged higher risk that DS subjects show of developing leukaemia, as compared to healthy subjects [14,15].

Sexual maturity in DS individuals is not accompanied by the rapid growth speed, which is typically observed in tegnered controls. Skeletal maturation is, instead, advanced in relation to height, with a relatively premature ossification of the growth cartilages. Such advanced age at puberty reverses the trend in bone maturation, which is reported to be slightly delayed in prepubertal patients with DS [14]. Short stature in DS children is not a harmonic feature: it is, instead, characterized by short lower limbs, with larger trunk and longer upper limbs. Deficient growth is particularly evident in children with DS and severe heart disease [9]. A recent Dutch study demonstrated that mean final height in DS subjects is 163.4 cm in boys and 151.8 cm in girls [15]. Final height is reached at a relatively early age both in boys (16 years) and in girls (15 years).

Regarding body weight growth, in the first life decade weight to height ratio in children with DS has been reported to be similar to that of healthy age-matched controls. Starting from the second decade, overweight is observed in about 50% of children with DS, in both sexes, which should be carefully monitored. In fact, overweight prevalence, as the increase in body mass index – in DS individuals is more frequent in children with DS [1] and their presenting symptoms can be growth failure and delay of puberty because of poor food intake, increased caloric utilization and consequent abnormal neuroendocrine regulation of growth and puberty [2,3]. A prompt diagnosis and an appropriate therapy can reduce comorbidities and allow adequate catch-up growth/weight and pubertal development. Since growth in children with DS differs markedly from that of normal children, the use of DS specific growth charts is important for diagnosis.

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assessed by using body mass index (BMI) > 27.8 kg/m² for males and > 27.3 kg/m² for females, was found more commonly among DS children than among the healthy population: 45% versus 33% among males and 56% versus 36% among females, respectively, according to one of the earliest studies addressing this topic in DS subjects. Average weight of adult patients with DS was calculated to be 71 kg for males (BMI 28.8 kg/m²) and 64 kg for females (BMI 30.8 kg/m²). Higher frequency of overweight is mainly determined by genetic factors, in particular DS subjects have decreased resting metabolic rates, as well as by constant hunger and excessive food intake. Women with DS had lower total leptin, an important regulator of food intake produced by fat cells. This finding may indicate a possible role of the free-bound leptin balance in the pathogenesis of obesity in DS [16,17].

In DS subjects puberty occurs at an unusually early age, as compared to healthy individuals [9]. Both primary and secondary sex characteristics in DS subjects showed the same developmental pattern noted in youngsters without DS [18]. The same goes for female adolescents with DS, who have a normal and regular menstrual cycle without significant difference in the average age of menarche among female adolescents with DS (13.8 years), as compared to healthy adolescents (13.6 years) [18]. Women with DS experience menopause at an earlier age (47.1 years), as compared to women with other mental disabilities without DS (49.3 years), and women without mental retardation (51 years) [18,19]. Men have low serum follicle-stimulating hormone concentrations, small testes and negative correlation between luteinizing hormone and testicular volume indicating primary gonadal insufficiency [14,20,21] (Figure 1).

References

Figure 1: Comparison between WHO child growth standards 2007 (5-19 years) and Cronk 1988 growth charts relating to subjects with DS (1 month-18 years) [21,12].