

Growth of children and adolescents with Down's syndrome. A brief review of the literature

Crescimento de crianças e adolescentes com Síndrome de Down – Uma breve revisão de literatura

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Abstract – Physical growth is one of the most important aspects of child and adolescent growth. Measurements of weight and height using specific charts for each population are needed to adequately monitor growth. The aim of this study was to review the literature regarding growth curves for individuals with Down's syndrome (DS). Sources of the primary and secondary literature were reviewed searching the following databases: CREUSP, PubMed, Medline, and section libraries of UNICAMP. The results showed an approximate growth of -1.5 to -4 standard deviations in subjects with DS when compared to the general population, with this difference starting during the prenatal period and extending into adulthood. No major differences were found between studies conducted in different countries. In conclusion, patients with DS present growth retardation when compared to the general population, resulting in shorter final height.

Key words: Growth charts; Children; Adolescents.

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Resumo – O crescimento físico é um dos mais importantes aspectos a serem considerados na saúde de crianças e adolescentes. E para um adequado acompanhamento do crescimento são necessárias avaliações de peso e estatura, utilizando-se gráficos provenientes de cada população em questão. O objetivo do presente estudo foi realizar uma revisão da literatura sobre curvas de crescimento de sujeitos com Síndrome de Down (SD). Foram revisadas fontes de literatura primárias e secundárias, através das ferramentas de busca: CREUSP, PUBMED, MEDLINE e bibliotecas setoriais da UNICAMP. Os resultados demonstram um crescimento aproximado em -1.5 a -4 desvios padrão em sujeitos com SD, quando comparado à população típica, iniciada esta diferença durante a fase pré-natal e se estendendo até a idade adulta. Não ocorrendo alterações de grandes amplitudes entre estudos de diferentes nacionalidades. Com isso, conclui-se que o crescimento de sujeitos com SD apresenta valores menores quando comparados à população típica, resultando em uma estatura final inferior.

Palavras-chave: Síndrome de down; Curvas de crescimento; Crianças; Adolescentes.



INTRODUCTION

Down's syndrome (DS) is a genetic disorder that was described by John Langdon Down more than a century ago¹. The disease is characterized by the presence of an extra chromosome that alters motor, physical and intellectual development²⁻⁴. It is one of the most frequent causes of intellectual disability, accounting for about 18% of all cases of intellectual deficiency seen at specialized educational facilities and rehabilitation centers in Brazil⁵.

DS is identified by fetal karyotyping performed in the first months of pregnancy and can manifest in three ways: simple nondisjunction in 95% of cases, translocation of chromosome 21 in 4%, and mosaicism in 1%⁶. The nondisjunction that causes trisomy 21 originates from the egg in 95% of cases and from the sperm in 5%⁷.

Epidemiological data show an incidence of DS of 1 in 600 live births in Brazil^{8,9} and the Brazilian regular education system includes children with disabilities. The inclusive education movement has been gaining grounds worldwide as the result of the UNESCO World Conference on Special Needs Education held in 1994, when the Salamanca Statement was adopted and education was discussed as a human rights issue^{10,11}. In Brazil, this movement also started in the 1990s and is supported by the 1988 Federal Constitution and by the Law of Directives and Bases of National Education No. 9.394/96, which establish that everyone has the right to education and that individuals with disabilities should attend regular education classes^{11,12}.

As a consequence, the participation of children with DS in the regular education system will become increasingly more common and physical education teachers will require appropriate and specific parameters to evaluate these children. In this respect, considering the importance of anthropometric data for the assessment of health,

nutritional status and growth of children and adolescents, we reviewed the literature regarding growth charts for subjects with DS in order to offer updated information to professionals working in this area.

METHODOLOGICAL PROCEDURES

The present study is a qualitative literature review, in which books, doctoral and Master's theses and articles of the Pubmed (www.pubmed.com), Scopus (www.scopus.com) and CREUSP (bibliotecas-cruesp.usp.br) databases, and the section libraries of UNICAMP (libdigi.unicamp.br), comprising the period from 1920 to 2009, were searched. Health-related databases were chosen in view of the objective of the study. The following keywords were used for the search: Down syndrome, trisomy 21, mongolism, growth charts. The studies identified were screened for investigations evaluating the growth of children and adolescents with DS and are shown in Table 1.

After identification of the studies, the abstracts were read and studies considered to be relevant were read in full and filed. Theses, dissertations and monographs were also included because of the scarcity of studies on the subject. Thirty-seven studies were included in this review. Only 10 of these investigations were specifically dealing with growth charts, whereas the remaining ones investigated variables that may influence the physical growth of children and adolescents with DS. The following parameters were used for analysis of the studies: methodology, age group, sample size, place of data collection, and growth-associated variables. The main characteristics of the studies that developed specific growth charts for children and adolescents with DS are summarized in Table 2.

Table 3 shows the gestational age and mean birthweight of subjects with DS.

Table 1. Studies identified during the database search using combinations of the respective keywords.

	DS	DSG	DSGC	T21	T21G	T21GC	M	MG	MGC
Pubmed	19,323	921	17	3,557	227	0	23,356	39	0
Scopus	23,283	1,248	27	5,655	401	7	627	18	0
CRUESP	132	2	1	18	1	0	32	0	0
UNICAMP	41	2	2	6	0	0	0	0	0
Total	36,303	1,801	36	4,018	228	0	23,721	45	0

DS = Down syndrome; DSG = Down syndrome + growth; DSGC = Down syndrome + growth chart; T21 = trisomy 21; T21G = trisomy 21 + growth; T21GC = trisomy 21 + growth chart; M = mongolism; MG = mongolism + growth; MGC = mongolism + growth chart.

Table 2. Characteristics of the studies that developed growth charts for children and adolescents with Down's syndrome.

Reference	Population	Sample size	Type of curve	Type of population	Age (years)
Cronk ¹³	American	90	Percentile	With associated illnesses	0 to 3
Cronk et al. ¹⁴	American	730	Percentile	With associated illnesses	0 to 18
Piro et al. ¹⁵	Sicilian	382	Mean and SD	Without associated illnesses	0 to 14
Cremers et al. ¹⁶	Dutch	284	Mean and SD	Without associated illnesses	0 to 20
Fernandes et al. ¹⁷	Portuguese	196	Mean and SD	Without associated illnesses	0 to 4
Styles et al. ¹⁸	United Kingdom and Republic of Ireland	1089	Percentile	With associated illnesses	0 to 18
Myrelid et al. ¹⁹	Swedish	354	Mean and SD	With associated illnesses	0 to 18
Mustacchi ²⁰	Brazilian	174	Mean and SD	Without associated illnesses	0 to 8
Kimura et al. ²¹	Japanese	85	Mean and SD	Without associated illnesses	0 to 20
Meguid et al. ²²	Egyptian	350	Mean and SD	With associated illnesses	0 to 3

SD = standard deviation.

Table 3. Comparison of gestational age and mean birthweight between subjects with Down's syndrome and the typical population.

Group	No. of cases	Gestational age (weeks)	Mean birthweight (g)
Control	3,011	39.75	3,324
Down's syndrome	180	38.78	3,007

Marcondes²³.

RESULTS

With respect to studies identified in books, Marcondes²³ investigated the growth of subjects with DS from the prenatal period to adult age. The author reported that infants with DS present a lower mean weight and shorter stature at birth than newborns without DS. In addition, newborns with DS tend to be slightly premature (less than 37 weeks of gestation) and are born on average 7 to 10 days before the predicted date, with the body weight of these infants being lower than expected for their gestational age as shown in Table 3. Marcondes²³ also found that subjects with DS continue to present a short stature throughout life. However, the degree of short stature varies according to age due to wide variations in growth velocity, with most of these subjects being -2 to -3 standard deviations below the reference population.

Batshaw and Perret²⁴ described different characteristics associated with DS, which are illustrated in Figure 1. The authors found a high incidence of factors that can influence the growth of subjects with DS, such as hypothyroidism and heart problems. An important fact indicated by the authors is the presence of short stature in 100% of subjects with DS and of obesity in 50%. One important study identified among dissertations and theses retrieved from the section libraries of UNICAMP and from the CRUESP system is the investigation of Zan Mustacchi²⁰, who developed weight-height reference curves for children with DS from the urban region of the city of São Paulo. This is the first growth chart for the Brazilian population with DS. For children from birth to 24 months of age, the author found a mean height of 83 cm for boys with DS compared to 87 cm for the control group. For girls with DS, the mean height was 81 cm versus 86 cm for the typical population. At 8 years, this difference was 10 cm for boys and 4 cm for girls. One limiting factor of that study was the age range of the subjects studied, which did not include the pubertal period.

Growth curves of children and adolescents with DS

The growth of subjects with DS has been studied for more than 80 years, with the pioneering

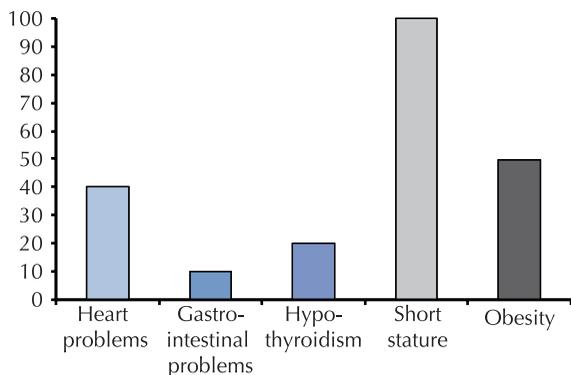


Figure 1. Characteristics of subjects with Down's syndrome reported by Batshaw and Perret²⁴.

studies of Brosseau and Brainerd²⁵, Benda²⁶ and Oster²⁷ who demonstrated a reduction in height of approximately one standard deviation.

One of the first growth charts for children with DS adopted worldwide was developed by Cronk et al.¹⁴ for the American population. The authors collected body weight and height data for children aged 1 month to 18 years and demonstrated a reduction of approximately 20% between the 3rd and 36th month of life for both genders, of 5% between 3 and 10 years for girls, and of 10% between 3 and 12 years for boys. During puberty, a reduction of 27% was observed for girls aged 10 to 17 years and of 50% for boys aged 12 to 17 years. These findings suggest that the growth spurt during puberty (peak growth velocity) is less vigorous in subjects with DS when compared to those without DS. This phenomenon was observed by Rarick and Seefeldt²⁸, who demonstrated that peak growth velocity is slightly reduced in subjects with DS. Cronk et al.¹⁴ also found that the increase in body weight exceeds height gain, resulting in an elevated body mass index. This fact may explain the high incidence of overweight and obesity among subjects with DS. With respect to DS subjects with heart problems, the authors showed a reduction in height and body weight of approximately 2 cm and 1 kg, respectively.

Since physical growth is one of the most important child health indicators, after the proposal of Cronk et al.¹⁴, other studies developing growth charts for children and adolescents with DS were conducted in different countries, such as Sweden, Japan, United Kingdom, Republic of Ireland, Sicily, The Netherlands, and Egypt, among others. For the development of growth charts for children and adolescents with DS in Sicily, Piro et al.¹⁵ evaluated body weight, height and head circumference data obtained between 1977 and 1988 from 382 children

aged 0 to 14 years, including 239 boys and 143 girls. All children seen during the same period who had some associated disease, such as congenital heart disease, hypothyroidism and gastrointestinal malformation, were excluded. The results showed growth deficits in children with DS compared to those without DS.

In a study conducted in The Netherlands¹⁶, growth charts were based on 2045 body weight and height records from 295 children with DS of both genders obtained from birth to 20 years of age. The authors obtained higher values than those reported in the American study conducted by Cronk et al.¹⁹. These differences may reflect genetic and environmental influences and indicate the need for the development of growth charts for each country. However, comparison of the typical Dutch population and with DS data showed a height deficit of -2.0 standard deviations. With respect to body weight, the weight/height ratio was above the 90th percentile after 10 years of age when compared to children without DS.

The growth curve of Portuguese children with DS was developed based on the evaluation of 198 subjects with DS (107 boys and 91 girls aged 0 to 48 months, corresponding to approximately 32% of Portuguese children with DS¹⁷). The results showed significant differences between children with DS and the typical population for all somatic parameters analyzed and for all age groups. Comparison of mean body weight and height between Portuguese and American children revealed similar results until 24 months of age. After this age, Portuguese children presented slightly higher values than American children, probably because of secular trends in growth since the American study was conducted in 1988 and the Portuguese study in 2001.

In a study conducted in Sweden, Myrelid et al.¹⁹ evaluated body weight, height and head circumference in 354 children and adolescents with DS from birth to 18 years. The results showed a lower growth velocity when compared to the typical population from birth to adolescence, particularly during the period from 6 months to 3 years and during the pubertal period. Height after birth and final height at 18 years corresponded to -1.5 and -2.5 standard deviations, respectively, when compared to the typical growth in Sweden. The authors observed that subjects with DS reached final height early when compared to the control group (16 years for boys and 15 years for girls), in agreement with previous studies^{14,29}. Regarding the pubertal period,

peak growth velocity was lower in subjects with DS, a fact contributing to a lower final height.

Another study that developed growth charts for subjects with DS was conducted in the United Kingdom and Republic of Ireland¹⁶. The authors analyzed the body weight, height and head circumference of 1089 children and adolescents with DS from birth to 18 years of age, including 597 boys and 492 girls. With respect to body weight, 30% of the sample older than 10 years presented a body mass index above the 91st percentile and 20% above the 95th percentile when compared to the typical population. The authors also observed a lower peak growth velocity in subjects with DS, resulting in lower height gains (cm/year) during puberty and in a lower final height compared to the typical population.

For the Japanese population with DS, Kimura et al.²¹ evaluated 85 children (43 boys and 42 girls) born between 1973 and 1985. Children diagnosed with mosaic DS and associated diseases were excluded from the study. The results showed that final height was lower in subjects with DS compared to the group without DS. The final height was 1.53 m for boys and 1.41 m for girls versus 1.69 and 1.57 m for the control group.

Meguid et al.²² developed growth charts and growth velocity curves based on 1700 body weight, height and head circumference records from 350 Egyptian children with DS aged 0 to 36 months, including 188 boys and 162 girls. Children with mosaic and translocation DS were excluded from the study. The assessments were performed at three

monthly intervals and the data were compared to those obtained for Egyptian children without DS of the same age during visits to Cairo hospitals. The children were divided into two groups: group 1 consisted of 260 children without congenital heart diseases (143 boys and 117 girls) and group 2 consisted of 90 children with mild to moderate congenital heart disease (45 subjects of each gender). Groups 1 and 2 presented a lower body weight, height and head circumference when compared to the population without DS. In boys of group 1, mean body weight was reduced by -1.5 standard deviations, height by -1.6 standard deviations, and head circumference by -1.8 standard deviations. In girls, these values were -1.6, -1.7 and -1.8 standard deviations, respectively. In contrast, much lower mean body weight, height and head circumference values were observed in boys of group 2 (associated congenital heart disease) when compared to group 1 and the control group, with a reduction of -2.8, -2.2 and -1.8 standard deviations, respectively. A similar trend was observed in girls, with a reduction of -2.8, -2.9 and -1.9 standard deviations for body weight, height and head circumference, respectively.

DISCUSSION

According to the theoretical framework reported, children with DS present a growth deficit that starts during the prenatal period and extends into adult life. This growth deficit shows similar in subjects with DS and no wide variations are observed

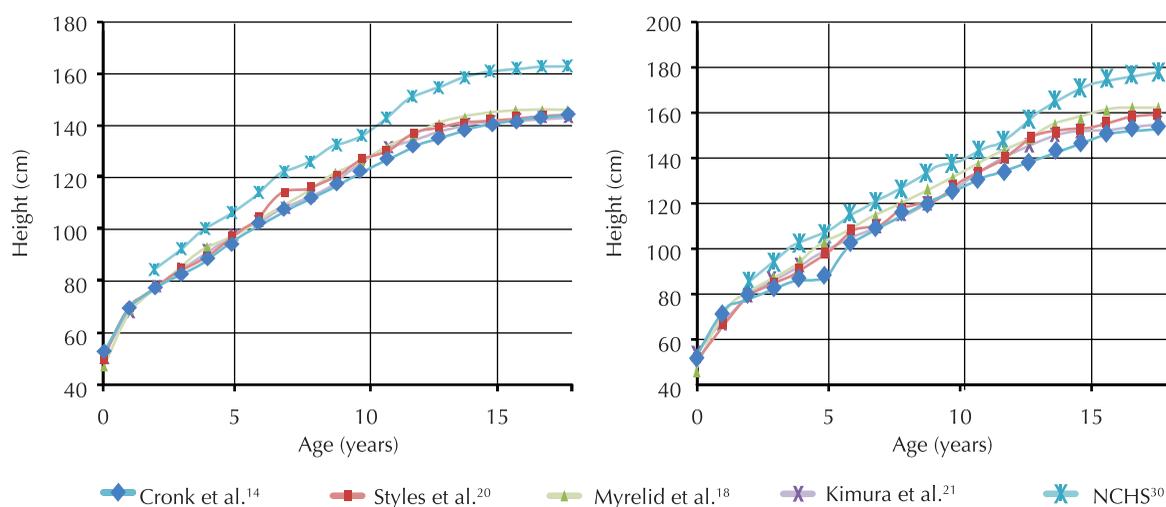


Figure 2. Growth curves obtained for girls (left) and boys (right) with Down's syndrome compared to the growth curve developed by the NCHS³⁰.

between studies conducted in different countries. This fact is illustrated in Figure 2, which shows the growth of subjects with DS from birth to 18 years of age reported in different studies compared to the typical population.

The growth curves illustrated in Figure 2 demonstrate the influence of puberty on the growth of children and adolescents with DS. As can be seen, the difference in height growth between subjects with DS and the typical population was relatively constant until the period of the growth spurt. When reaching the growth spurt, height gains (cm/year) were lower in the population with DS, increasing the difference to the typical population and resulting in a lower final height.

One of the factors that possibly influence the growth retardation of subjects with DS is a deficiency in insulin-like growth factor 1 (IGF-1), the main factor responsible for the actions of growth hormone (GH). IGF-1 is mainly produced by the liver and stimulates cell proliferation and somatic growth²⁹. Another study³¹ analyzed the effects of treatment with GH on the growth of subjects with DS. The 6-month growth rate increased from 2.3-2.8 cm to 3.3-5.8 cm. A higher concentration of IGF-1 was also observed after treatment with GH, but the gains were lower than those reported for the typical population. Similar results have been reported in a study following up 15 children with DS treated with GH for 3 years from the age of 6-9 months³². The mean height of children treated with GH increased, with a reduction in the distance to the 50th percentile of the typical population (-1.8 standard deviations before and -0.8 standard deviations after treatment compared to the Swedish standard). The low serum concentrations of IGF-1 became normal during treatment. However, the growth velocity declined after the discontinuation of treatment.

Zinc deficiency is another factor that may influence the growth and development of children with DS since this nutrient plays an important role in child development and growth. According to Wilke³³, zinc supplementation in children with mild deficiency increases appetite, growth velocity and GH, somatomedin and IGF-1 levels, and improves immunity. Zinc supplementation for 6 to 9 months was analyzed in 22 children with DS³³. During this period, the growth percentile increased in 68% of the sample. The growth velocity was practically twice as high and there was an increase in the plasma levels of GH and somatomedin. Similar

findings have been reported in other studies^{9,35,36} investigating zinc concentration in children with DS, which found a significant difference compared to the control group.

The growth deficit observed in children with DS can also be explained by the presence of heart problems³⁷, upper airway obstruction during sleep³⁸, celiac disease³⁹, thyroid deficiency⁴⁰, and inadequate nutrition due to feeding problems generally observed in subjects with DS.

With respect to growth, there is consensus in the literature that children and adolescents with DS present a height deficit when compared to the typical population. This difference starts during the prenatal period and extends into adult life. This growth deficit is similar in subjects with DS and no wide variations are observed between studies conducted in different countries^{14-18,20,21}.

CONCLUSIONS

The differences between studies investigating the growth of children and adolescents with DS impair the clinical characterization and assessment of weight-height development of these subjects. Some studies exclude subjects with mosaic or translocation DS, congenital heart diseases and associated diseases, whereas others do not adopt these exclusion criteria. Another limiting factor is the method adopted for the development of growth charts, with some studies using the mean and standard deviation, whereas others classify the subjects according to percentile. However, it is accepted that the mean height of boys and girls with DS is reduced by approximately 1.5 to 4 standard deviations, i.e., less than the 5th percentile. The largest growth deficits occur during the first years of life and during puberty.

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