Chapter 4

Prevalence of overweight in Dutch children with Down syndrome

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Abstract

Objective: Prevalence of overweight in children is increasing, causing various health problems. This study aims to establish growth references for weight and to assess the prevalence rates of overweight and obesity in a nationwide sample of Dutch children with Down syndrome (DS), while taking into account the influence of comorbidity.

Patients and Methods: In 2009, longitudinal growth data from Dutch children with Trisomy 21 who were born after 1982 were retrospectively collected from medical records of 25 Dutch regional specialized DS centers. 'Healthy' was defined as not having concomitant disorders or having only a mild congenital heart defect. Weight and body mass index (BMI) references were calculated using the LMS method, and prevalence rates of overweight and obesity using cut-off values for BMI as defined by the International Obesity Task Force. Differences in prevalence rates were tested by multi-level logistic regression analyses to adjust for sex and age.

Results: Growth data of 1,596 children with DS were analyzed. Compared to the general Dutch population, healthy children with DS were more often overweight (25.5% vs. 13.3% in boys, and 32.0% vs. 14.9% in girls) and obese (4.2% vs. 1.8%, and 5.1% vs. 2.2%, respectively). Prevalence rates of overweight between DS children with or without concomitant disorders did not vary significantly.

Conclusions: Dutch children with DS have alarmingly high prevalence rates of overweight and obesity during childhood and adolescence. Health care professionals should be aware of the risk of overweight and obesity in children with DS, to prevent complications.

What's known on this subject

- Some groups of children are especially prone to develop overweight and obesity.
- Overweight in children affects their physical and psychological health, and shortens life expectancy.
- Overweight in children with Down syndrome is attributed to their commonly found comorbidities.

What this study adds

- Prevalence rates of overweight and obesity in a nationwide sample of otherwise healthy children with Down syndrome.
- Overweight is observed from very young ages in healthy children with Down syndrome and those with severe congenital heart defects.

Introduction

The worldwide increase in the prevalence of overweight and obesity in children is alarming.[1] Overweight and obesity are even more common in children with Down syndrome (DS). One third to one half of children with DS are overweight. These rates vary because of differences in study population, methods and cut-off values used in the studies.[2-6]

Overweight and obesity cause both psychological and physical health problems in children, such as low self-esteem, depressive symptoms, lower general physical condition, and metabolic complications. It is not known whether all these consequences of overweight and obesity in children in the general population are to be expected in children with DS, because no data have yet been published on the effect of overweight and obesity in children with DS. Another consequence of overweight and obesity in children is the increased risk of becoming obese adults, which means having an increased risk for cardiovascular diseases, musculoskeletal disorders, and metabolic disorders at an older age. Because of the shorter life expectancy, it is doubtful whether these full complications will occur among people with DS. One study of adults with DS showed that obesity appears to play an important role in the pathophysiology of obstructive sleep apnea: the apnea hypopnea index was highly correlated with the degree of obesity.[7,8] However, it is very plausible that complications such as poor general physical condition and musculoskeletal disorders will occur in children with DS.

Up to now, many explanations for the higher prevalence of overweight and obesity in DS were based on the presence of concomitant disorders. Hypothyroidism for example is more common in children with DS and predisposes to increased body weight.[9,10] Therefore, it is important to know the prevalence of overweight and obesity in children with DS, not only generally but also separately for those children with and without comorbidity. Children with DS have a high risk of concomitant disorders that are known to influence body weight both positively as well as negatively.[11-13] This study aims to establish specific growth references for weight in children with DS, and to assess the prevalence rates of overweight and obesity in a nationwide sample of Dutch children with DS, while taking into account the influence of comorbidity.

Methods

Data were collected from medical records of children attending one of the hospital-based regional outpatient clinics for children with DS in the Netherlands. All these clinics were approached for participation in order to collect representative nationwide data. Between July 2009 and February 2010 the first author visited the participating clinics and collected retrospective anonymous data on growth from 2000 onwards, medical conditions and background information. Additionally, some child health physicians involved in the care of adolescents with DS supplied data by completing standard forms. Because all children

visit one of these clinics providing standard medical care for children with DS using a well-defined screening program, their health status is accurate.[14]

Dutch children with Trisomy 21 karyotype and born after 1982 were selected. Growth data included measurements of weight, height and head circumference. In this study only weight and BMI are discussed. Full details of data collection were presented in our previous paper on healthy growth in children with DS.[15] The children were categorized into four health categories (see also Table 4.1): 1. 'healthy': no concomitant disorders and negative screening results or only mild congenital heart defect (CHD) (hemodynamic stable); 2. severe CHD (hemodynamic unstable and needing surgical intervention or medication or having pulmonary vascular disease); 3. hypothyroidism; 4. other disorders and treatments known to influence growth, and children with multiple concomitant disorders. Because our previous study demonstrated children without concomitant disorders or with only mild CHD have the same growth pattern,[15] these children are pooled to form the healthy category . The new growth references established in this study as well as the prevalence rates were based on measurements of this otherwise healthy group of children.

Table 4.1: *Characteristics of the various health categories in the study population*

Healthy	
	Children without concomitant disorders that could possibly interfere with growth or children with hemodynamic stable CHD (not needing surgical intervention or medication and without pulmonary vascular disease)
	Children with negative screens for celiac disease and hypothyroidism
	For example: children with cataract were included and children with musculoskeletal disorders were excluded; children with an atrial septal defect or patent foramen ovale without complaints were included
Severe CHD	
	Children with hemodynamic unstable CHD (needing surgical intervention, medication, or with pulmonary vascular disease)
	For example: children with an atrioventricular septal defect or Tetralogy of Fallot
Hypothyroidism	
	Children with hypothyroidism: congenital or acquired
	For example: hypothyroidism confirmed after positive screening
Other disorders	
	Children with other disorders and treatments known to interfere with growth, and children with multiple concomitant disorders
	For example: children with congenital gastrointestinal malformations, celiac disease, leukemia or diabetes, children on anti-epileptic medication or corticosteroids (including inhalation medication)

Abbreviations: CHD – congenital heart defect

Statistical Analysis

All measurements of children with one or more outlying measurements were excluded. Outliers were defined as standard deviation scores (SDS) >4 or <-6 for weight, >5 or <-7

for birth weight, and >2 or <-6 for height, using the age and sex-specific references of the general Dutch population (Fourth Dutch Growth Study, 1997).[16] BMI was calculated as weight/height^2 and expressed as kg/m^2.

Specific reference charts for weight-for-age were established for children with DS up to the age of 15 months. Reference charts reflect the range of normal growth of a healthy child. However, the present distribution of weight in the population at older ages is not something to be aimed for, because of the current increase in the proportion of children with obesity.[17-19] Therefore, references for weight-for-age are plotted in this study only for the younger ages where there still is a normal distribution of weight. References were constructed by using the LMS method, which summarizes the distribution by three age-dependent smooth curves representing the skewness (L curve), median (M curve) and coefficient of variation (S curve).[20] The references were fitted in R Version 2.9.0 using Generalized Additive Models for Location Scale and Shape (GAMLSS).[21] A log transformation of age was applied to expand the ages where growth velocity is high and compress ages where growth velocity is low. Worm plots were used as a diagnostic tool for visualizing how adequate our models fitted the data.[22]

Prevalence rates of overweight and obesity were calculated separately for boys and girls with DS within the various health categories. To obtain accurate prevalence rates, cut-off values for BMI as defined by the International Obesity Task Force were used on the LMS parameters of BMI distribution in the DS study sample.[23] All overweight rates in this paper include obesity. The prevalence rates were compared between children with DS within the various health categories, and were compared with the prevalence rates of overweight and obesity of children in the general Dutch population (Fifth Dutch Growth Study, 2009).[17] Multi-level logistic regression analyses, adjusted for sex and age, were performed to test the differences in prevalence rates of children with DS within the various health categories.

Table 4.2: *Number of children and measurements for weight of 1,596 Dutch children with Down syndrome, specified by health categories*

	Number of subjects			Number of measurements	
Health category	**n**	**Boys**	**Girls**	**Boys**	**Girls**
Healthy or only mild CHD	664	387	277	2404	1776
Severe CHD	269	114	155	864	1169
Hypothyroidism*	119	60	59	402	541
Other disorders	544	330	214	2944	1836
Total	1,596	891	705	6,614	5,322

Abbreviations: CHD – congenital heart defect
* including mild CHD

Results

Growth data of 1,596 Dutch children with Trisomy 21 were collected from medical records of 25 specialized DS clinics (83% of all DS clinics in the Netherlands) and from the participating youth health care physicians. This sample included 891 boys (55.8%) and 705 girls, with 6,614 and 5,322 measurements for weight respectively. Table 4.2 shows the number of subjects and weight measurements, specified by the various health categories. The major group is formed by the otherwise healthy children (41.6%). The children with severe CHD represent 16.9%, the children with hypothyroidism represent 7.5%, and the category with various other disorders represent 34.1%.

Table 4.3: *New weight (kg)-for-age references for 0-15 months in Dutch children with Down syndrome: values of L (skewness), M (mean), and S (coefficient of variation)*, arranged by age and sex.*

	Boys			Girls		
Age (weeks)	**L**	**M**	**S***	**L**	**M**	**S***
0	1.06	3.05	.1930	.91	3.03	.1471
2	1.05	3.36	.1848	.86	3.27	.1443
4	1.03	3.66	.1773	.82	3.51	.1418
6	1.02	3.97	.1706	.79	3.79	.1395
8	1.00	4.29	.1645	.75	4.07	.1375
10	.99	4.62	.1590	.73	4.36	.1357
12	.97	4.95	.1541	.70	4.64	.1342
16	.94	5.58	.1460	.67	5.17	.1316
20	.91	6.15	.1395	.64	5.67	.1295
24	.89	6.65	.1345	.62	6.13	.1277
28	.87	7.08	.1304	.62	6.55	.1262
32	.84	7.47	.1270	.63	6.92	.1246
36	.81	7.82	.1240	.63	7.25	.1231
40	.77	8.13	.1213	.65	7.55	.1216
44	.72	8.42	.1188	.67	7.83	.1201
48	.66	8.70	.1165	.69	8.09	.1186
52	.60	8.95	.1143	.70	8.34	.1172
56	.53	9.19	.1122	.72	8.55	.1158
60	.50	9.41	.1103	.74	8.76	.1144
65[a]	.39	9.67	.1080	.76	9.00	.1127

[a] Corresponding with 15 months.
* Individual weight SDS can be calculated by: SDS (SD) = ((weight (kg)/M)^{L} -1) / L*S.

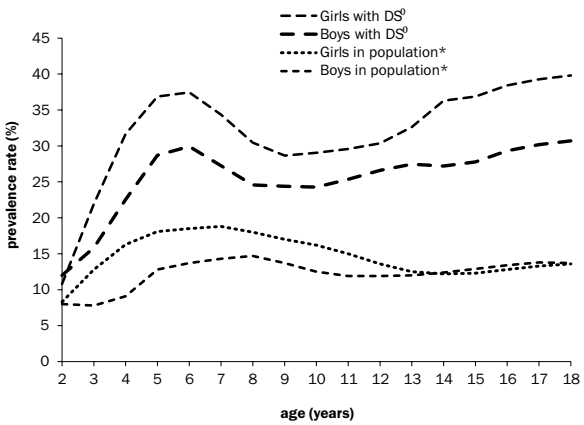
Growth references for weight-for-age were plotted for the age of 0-15 months based on 199 boys and 156 girls; yielding 959 measurements for boys and 761 for girls. Table 4.3

summarizes the LMS values, arranged by age and sex. Mean birth weight was 3.1 kg for boys and 3.0 kg for girls with DS. Compared with the general Dutch population (1997) mean birth weight of children with DS was 1.1 SD lower in boys and 0.9 SD lower in girls. At the age of 15 months, mean weight was 9.7 kg for boys and 9.0 kg for girls, respectively 1.1 SD and 1.2 SD lower than in the general population.

Prevalence rates of overweight and obesity in otherwise healthy children with DS are presented in Table 4.4. The prevalence rates of overweight are also shown in Figure 4.1. For comparison, the prevalence rates in children from the general population are also shown in this table and figure. In total, 25.5% of the boys with DS and 32.0% of the girls were overweight. Obesity was observed in 4.2% of the boys and 5.1% of the girls with DS. The prevalence rates were roughly constant over the age ranges: from the age of four years more than one quarter of the children were overweight. Compared with the general Dutch population, prevalence rates in children with DS were on average twice as high for both overweight and obesity. The rapid increase in prevalence of overweight between the age of two and six years is striking. This increase is clearer in children with DS than in children from the general population.

Prevalence rates of overweight of children with DS vary between children within the various health categories. Although children with DS and severe CHD showed almost the same prevalence rates of overweight (28.1%), the children in the category with hypothyroidism showed higher rates (35.1%). However, after correcting for sex and age, these differences were not significant.

Figure 4.1: Prevalence rates (%) of overweight in otherwise healthy children with Down syndrome (n=659), compared to children in the general population, arranged by sex and age.*



[0] DS = Down syndrome

* General population: prevalence rates of the Fifth Dutch Growth Study in 2009 [17]

Discussion

This study presents prevalence rates of overweight and obesity in a nationwide population based sample of almost 1600 Dutch children with DS. A strict selection on the basis of health status of the children resulted in data based on a group of otherwise healthy children with DS. The approach of dividing the children into various health categories based on co-morbidity that can influence their growth (height and/or weight) is an important part of this study, and provides information on the presence of overweight and obesity in children within these various health categories. It is not only healthy children with DS who have a high prevalence of overweight and obesity, but also the children with any type of co-morbidity. Prevalence rates of overweight and obesity vary between children with DS in the different health categories, but no statistically significant differences were observed.

Table 4.4: *Prevalence rates (%) of overweight and obesity in otherwise healthy children with Down syndrome (n=659), compared to children in the general population*, arranged by age and sex.*

	Overweight				Obesity			
	Boys		Girls		Boys		Girls	
Age	DS[0]	Pop.*	DS	Pop.	DS	Pop.	DS	Pop.
2.0	12.0	8.0	10.8	8.3	2.0	0.7	1.0	0.7
3.0	15.9	7.8	22.0	12.8	2.7	0.8	2.9	1.6
4.0	22.6	9.1	31.7	16.3	4.5	1.1	5.3	2.6
5.0	28.7	12.8	36.9	18.1	6.5	2.0	6.9	3.3
6.0	29.9	13.7	37.4	18.5	6.5	2.1	6.8	3.4
7.0	27.2	14.3	34.4	18.8	5.3	2.1	5.2	3.4
8.0	24.6	14.7	30.5	18.0	4.5	2.2	3.9	3.2
9.0	24.4	13.7	28.7	17.0	4.1	2.0	3.3	2.8
10.0	24.3	12.5	29.1	16.2	3.8	1.7	3.3	2.5
11.0	25.4	11.9	29.6	15.0	3.7	1.6	3.5	2.1
12.0	26.6	11.9	30.4	13.6	3.7	1.6	4.0	1.8
13.0	27.5	12.0	32.6	12.5	3.7	1.6	5.0	1.6
14.0	27.2	12.4	36.3	12.2	3.6	1.7	6.6	1.5
15.0	27.8	12.9	36.9	12.3	3.7	1.8	6.7	1.5
16.0	29.3	13.4	38.4	12.8	4.2	1.9	7.2	1.6
17.0	30.2	13.8	39.3	13.3	4.4	2.0	7.4	1.7
18.0	30.7	13.7	39.8	13.6	4.5	1.9	7.5	1.7
2.0-18.0^	25.5	12.3	32.0	14.7	4.2	1.7	5.1	2.2

[0] DS = children with Down syndrome
* Pop. = General population: prevalence rates of the Fifth Dutch Growth Study in 2009 [17]
^ Mean prevalence rate for children aged 2-18 years

From the age of four over 25% of the healthy children with DS are overweight. The rapid increase in prevalence of overweight in children with DS between two and six years of age is striking, in boys as well as in girls (presented in Figure 4.1). In view of the fact that overweight children have an increased risk of becoming obese adults, such high prevalences are alarming, since this may lead to poor general physical condition, and comorbidity such as obstructive sleep apnea, musculoskeletal disorders, and cardiovascular diseases.[7,8,24,25] This emphasizes the importance of awareness of the occurrence of overweight in children with DS at very young ages.

New reference charts are established for weight-for-age for boys and girls with DS up to the age of 15 months and will aid appropriate monitoring. After the age of 15 months no reference charts specific for DS are established, because the present distribution of weight in the population at older ages is not something to be aimed for. In the Netherlands, normative growth charts for weight-for-height and BMI-for-age are used for children in general as well as for children with DS. The normative reference charts for BMI-for-age include international cut-off values for overweight and obesity, and for thinness grades 1 and 2.[17,23,26,27] All growth charts are available at www.tno.nl/growth. Additional research is needed to determine how sensitive and specific these international cut-off values are in children with DS. Until more information is available to improve monitoring, the currently available general weight and BMI charts will be used for growth monitoring in children with DS older than 15 months, and seems to work well with the specific weight-to-age charts for the age of 0-15 months.

Another important result is that children with DS with severe CHD show nearly the same high prevalence rates. During the early years of life of these children attention is mainly concentrated on their medical heart defect condition. However, our data show that it is also necessary to be aware of the need to prevent excessive weight gain. Our data indicate a higher prevalence of overweight and obesity in children with DS and hypothyroidism. This is somewhat surprising since all children with DS were screened for hypothyroidism, as advised in the guideline of the Pediatric Association of the Netherlands.[14] This means that hypothyroidism is diagnosed and treated at an early stage before complaints arise and weight gain is caused.

For optimal prevention and intervention more should be learned about the underlying cause of excessive weight gain in children with DS. One of the theories about this cause is resistance to leptin. This is a hormone excreted by adipocytes that suppresses appetite and regulates body weight. Leptin is positively correlated with body fat, so people with obesity have a type of leptin resistance.[28,29] Magge *et al*. have observed that leptin levels and the proportion of body fat were more positively correlated in children with DS than in their brothers and sisters.[30] The cause of this phenomenon is unknown. Other studies investigated the presence of reduced resting metabolic rate. Small studies showed some

support for this theory.[31] However, Fernhall et al. demonstrated no difference in metabolic rate between individuals with DS and control individuals of similar ages.[32] Another theory is based on the influence of lifestyle. Higher rates of overweight and obesity might be attributed to lesser physical activity or higher nutrient intake.[6,33-35] Nevertheless, the few available studies on these subjects do not as yet provide convincing evidence for any specific theory.

With the knowledge we have from studies among children in the general population, we assume that physical activity and feeding patterns are likely the essential factors influencing body weight in children with DS. Additional research is needed to establish the merit of this assumption and to explore other underlying factors. As long as the underlying causes are still unknown, a specific approach to tackle the cause is not possible. However, dietary factors and insufficient physical activity are considered to be main contributors to the development of overweight. Assuming that this also applies to children with DS, we expect that they will benefit from it. Children with DS often want to keep to a strict routine to optimize their autonomy. When a healthy diet and enough physical activity is a structural part of this personal daily routine, the children will probably adhere to such a routine. Therefore, appropriate information for parents and children is essential, and must be provided by youth health care workers and pediatricians. Parents need to know what a healthy weight is for their child with DS. With this in mind they can support their child to achieve and maintain a healthy weight. These approaches to prevent excessive weight gain are an important task for the professionals involved in the care for children with DS.

Conclusions

We observed an alarming prevalence of overweight and obesity in Dutch children with DS. Overweight and obesity are observed from a young age in otherwise healthy children with DS as well as in children with DS and severe CHD. Health care professionals should be aware of the risk of overweight and obesity in children with DS and should ensure that growth is monitored regularly in all children with DS, thus enabling early detection of inappropriate weight gain and starting appropriate interventions where necessary. In this way undesirable psychological and physical health consequences may be prevented. Parents and children also need appropriate information to prevent excessive weight gain. We expect that a structured healthy life style, including eating a healthy diet and having sufficient physical activity, will be especially effective in children with DS because of their tendency to follow a strict routine. Specific prevention programs to prevent excessive weight gain that are suitable for children with DS and support their families may be valuable.

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