Nutrición Hospitalaria

Nutr Hosp. 2015;31(6):2472-2478
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original / *Pediatría*

The distribution of the indicator height for age of Mexican children and adolescents with Down syndrome according to different reference standards

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Abstract

Objective: **to compare the indicator height for age in Mexican children with Down Syndrome (DS) with two different reference patterns of growth (American and Spanish) that might be suitable for the Mexican population.**

Methods: **a cross-sectional study was performed including 235 Mexican children and adolescents of both sexes with DS aged 45 days to 16 years enrolled in two specialized schools in the metropolitan area of Guadalajara. The dependent variables were weight/age; height/age; weight/height and BMI. The data expressed was percentiles and the chi-square test was used to compare the distribution of the height/age index with American and Spanish reference patterns. In addition, a chi-square test was performed for the goodness of fit of the height/age index, with breakpoints lower and greater than the 50th percentile.**

Results: **the percentage of participants who were below the 50th percentile in the height/age index was significantly higher with the Spanish vs. the American reference pattern. The chi-square test for goodness of fit showed that the frequency of cases located below the 50th percentile in the height/age index was significantly higher with the American pattern in the age groups of 0 to 36 months (p = 0.022) and 37 to 72 months (p <0.001), but it was not significant (p = 0.225) in the older than 72 months age group.**

Conclusion: **the American reference pattern is a better fit for the growth of Mexican children with DS compared with the Spanish reference pattern, and the distribution profile obtained with the standard growth and WHO reference was not suitable for the assessment of children with Down syndrome.**

(*Nutr Hosp*. 2015;31:2472-2478)

DOI:10.3305/nh.2015.31.6.8815

Key word: *Down syndrome. Height/age index. Reference pattern.*

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Recibido: 7-II-15.
1.ª Revisión: 8-III-15.
Aceptado: 15-III-15.

LA DISTRIBUCIÓN DEL INDICADOR TALLA PARA LA EDAD DE NIÑOS Y ADOLESCENTES MEXICANOS CON SÍNDROME DE DOWN DE ACUERDO A DIFERENTES PATRONES DE REFERENCIA

Resumen

Objetivo: **comparar el índice talla/edad en niños con síndrome de Down (SD) con dos patrones de referencia (americano y español) que podrían ser adecuados en niños mexicanos.**

Métodos: **en un estudio transversal se incluyeron 295 niños y adolescentes de ambos sexos con SD desde 45 días hasta 16 años de edad, inscritos en dos escuelas del área metropolitana de Guadalajara. Variables dependientes: peso/edad; talla/edad; peso/talla e IMC. Los datos fueron expresados en percentiles y se utilizó la prueba de chi-cuadrado para comparar la distribución del índice de talla/edad entre los patrones de referencia de EUA y de España. Se realizó una prueba de bondad de ajuste del índice talla/edad con puntos de corte menor y mayor al percentil 50.**

Resultados: **el porcentaje de participantes por debajo del percentil 50 en el índice de talla/edad fue significativamente mayor con la referencia española vs. americana. La prueba de bondad de ajuste mostró que la frecuencia de casos debajo del percentil 50 en el índice talla/edad fue significativamente mayor con la referencia estadounidense en el grupo de edad de 0-36 meses (p = 0,022) y 37-72 meses (p <0,001), pero no fue significativa en el grupo de edad mayor de 72 meses.**

Conclusión: **la referencia estadounidense se ajustó más al crecimiento de los niños mexicanos con síndrome de Down que la referencia española. El perfil de distribución obtenido con el estándar de crecimiento y referencia de la OMS no fue adecuado para la evaluación de niños con síndrome de Down.**

(*Nutr Hosp*. 2015;31:2472-2478)

DOI:10.3305/nh.2015.31.6.8815

Palabra clave: *Síndrome de Down. Índice talla/edad. Patrón de referencia.*

Introduction

Down syndrome (DS) is the most common chromosomal aneuploidy detected and the first known genetic cause of mental disability[1, 2]. It has an incidence of 1/1000 to 1/1100 live births worldwide[3] and Mexico has reported an incidence of 1/650 live births[2]. DS is associated with congenital malformations (especially heart), a characteristic phenotype and organ dysfunction. One problem in assessing children with DS is that their growth is markedly different compared with that of normal children, it is slower, and children with DS present with short height[4] and smaller head circumferences (HC)[5]. Because the growth of these children is affected in the uterus and after birth, the growth rate is mainly lower between six months and three years of age[6, 7]. However, this growth rate varies by countries where reference tables have been developed[7]. Mexico lacks a reference pattern for children with DS; therefore, considering that height is usually a good indicator of nutrition and health in childhood, the purpose of this study was to evaluate the indicator of height for age in Mexican children with DS using two different reference patterns for growth (American and Spanish) that might be suitable for the Mexican population.

Methods

This cross-sectional study included 235 children and adolescents of both sexes with DS aged 45 days to 16 years, who were enrolled in two specialized schools in the metropolitan area of Guadalajara: a) Integral Family Development Jalisco (public sector) and b) Down School of Guadalajara, AC (private sector) from June 2009 to February 2010. The inclusion criteria were: children with and without congenital heart disease, hypothyroidism and/or congenital malformations related to DS, children who tolerated anthropometric measurement and for whom written approval was provided by a parent or guardian.

Anthropometric variables: height/age; weight/age; weight/height and BMI (percentiles). Reference standards from the USA[6] and Spain[8], The WHO Child Growth Standards[9] and the growth reference data for children aged 5-19 years were used[10]. Distributions of the expected frequency of the height indicator for age with the three reference standards were developed. *Other variables:* socioeconomic and demographic characteristics such as the number and type of family members; age, education and occupation of parents; and employment status, monthly household income and spending power for food estimated per month and per capita as a percentage of the minimum wage per day were also obtained.

Anthropometric measurements

To measure anthropometric indicators, children and adolescents wore minimal clothes and were barefoot and without support. Weight: Health or Meter® high-chairs (Purvis, MS, USA) were used for children under three years or for children who could not stand. Children aged three and under seven were weighed on a scale Seca® 700 (Tecnigen, Hamburg, Germany). Children over seven years were weighed on a scale Tanita TBF-410 (Arlington heights, IL, USA).

Height. The length of children under three years of age was obtained using a Seca® 416 infantometer (Tecnigen, Hamburg, Germany). A stadiometer Seca 214 (Tecnigen, Hamburg, Germany) was used to obtain the height of children over three years old. Measurements were made by two different observers and the average of the two measurements was calculated. Before the anthropometric measurements were collected, the Habicht[11] standardization process was undertaken by the two participating observers.

Statistical Analysis

The frequencies and percentages of nonparametric variables and measures of central tendency parametric variables were determined. The data are expressed in percentiles, and the chi-square test was used to compare the distribution of the height/age index using the US[5] and Spanish reference patterns of growth[8]. The sample was divided into three age groups: 0-36 months, 37-72 months and over 72 months. In addition, a chi-square test was performed for the goodness of fit of the height/age indices with breakpoints lower and higher than the 50th percentile. The data were captured in Excel and analyzed using SPSS version 10.

Ethical Considerations

Adequate information was given to parents about the importance of this non-interventional study and signed informed consent from parents and/or persons legally responsible for the participants and the consent of the directors of the institutions were obtained.

Results

A total of 235 subjects with a predominance of males (57%) were included. By age group, preschoolers were the most frequent (43.5%), then infants (23.4%), schoolchildren (23.4%) and adolescents (9.7%). Most were of low-middle socioeconomic status and were from the metropolitan area of Guadalajara, table I. The schooling of the fathers and mothers was similar with 17% of each holding bachelor's degrees. In 60% of cases, the mothers were housewives.

Regarding the perinatal and medical history, 19.2% of participants were premature; 108 cases (46%) reported some type of heart disease; 29.6% were diagnosed with non-determined heart disease and 44.4%

Table I
Descriptive data of the participant socio-demographic and economic characteristics

Variable	*n*	*Mean*	*SD*	*Minimum*	*Maximum*
Number of family members	225	5.2	1.7	2	12
Number of living children	225	3.0	1.7	1	14
Place of the child	226	2.8	1.7	1	13
Mother's age (years)	222	36.1	8.5	16	55
Age when pregnant (years)	222	31.4	7.8	15	49
Father's age (years)	210	37.7	9.1	18	66
Maternal education (years)	220	9.9	4	0	24
Father's education (years)	203	9.9	4	0	22
Monthly family income ($)[1]	202	7531	7671	0	51000

[1]Mexican pesos. Rate peso/dollar 12.6/1

Tabla II
A comparison between the American reference pattern vs. the Spanish reference pattern using the indicator height for age (percentile) by age group.

Age (months)	*American*				*Spanish*				*p*
	<50		*>50*		*<50*		*>50*		
	n/N	*%*	*n/N*	*%*	*n/N*	*%*	*n/N*	*%*	
0-36	57/92	62	35/92	38	73/92	79	19/92	21	<0.001
37-72	15/75	20	60/75	80	61/75	81	17/75	19	<0.001
>72	29/68	43	39/68	57	47/65	72	18/65	28	<0.001

had a heart murmur. Upon evaluation, 56% of the heart disease diagnoses were correct. Other important pathologies were hypothyroidism (9%) and digestive congenital malformations (6.2%).

It was noted that according to the American anthropometric reference[6], 54% of children were below the 50th percentile of the weight/age index, while when using the Spanish anthropometric reference[8], 77.4% were below this percentile. When using the WHO weight/height index, 48.5% were below the 50th percentile and 12.3% were below the 3rd percentile. Regarding BMI, 50.1% were below the 50th percentile, 14% were below the 3rd percentile and 20.4% were above the 85th percentile.

It was observed that the percentage of participants who were below the 50th percentile in the height/age index was significantly higher using the Spanish reference pattern vs. the American reference pattern in the studied age groups, table II. The chi-square test for goodness of fit (observed/expected) showed that the frequency of cases located below the 50th percentile in the height/age index was significantly higher using the American pattern among the age group of 0-36 months ($p=0.022$), it was significantly lower in the age group of 37-72 months ($p<0.001$), but it was not significant ($p=0.225$) in the age group older than 72 months, table III.

It was observed that with the Spanish reference pattern the frequency of cases below the 50th percentile is significantly higher in all three age groups ($p<0.001$). Comparing the height/age index to the standard growth of 2006 and the WHO reference standard of 2007, table IV shows that in the three age groups 0-36 months, 37-72 months and older than 72 months most of the participants were below the 3rd percentile.

These findings are seen more clearly in figure 1, in which the percentile distribution of the expected frequency and distributions of the height/age index among the study population that are achieved using the American[6], Spanish[8] and WHO reference data from 2006[9] and 2007 are presented[10]. With the American reference pattern, the distribution of height/age is acceptably uniform; however, with the Spanish pattern

Table III
A comparison between the observed vs. the expected values using reference standards (American and Spanish) for Down syndrome for the indicator height for age (percentile) by age group

Age (months)		*American*					*Spanish*				
		Observed		*Expected*			*Observed**		*Expected*		
	N	*<50*	*>50*	*<50*	*>50*	*p*[a]	*<50*	*>50*	*<50*	*>50*	*p*[a]
0-36	92	57	35	46	46	0.022	0.022	73	73	46	<0.001
37-72	75	15	60	37.5	37.5	<0.001	<0.001	61	61	37.5	<0.001
>72	68	29	39	34	34	0.225	0.225	47	47	32.5	<0.001

*The Spanish references evaluate only until 15 years of age, so that in the group > 72 years changes the n = 65.
[a]Calculated with the X2 test for goodness of fit.

Table IV
The distribution of participants (n=235) by percentiles according to the standard growth 2006 and 2007 WHO reference pattern for the indicator height for age.

Age (months)	*N*	*< p3 (%)*	*≥ p3 and < p15 (%)*	*≥ p 15 and < p50 (%)*	*> p50 (%)*
0-36	92	58 (63.1)	21 (22.8)	12 (13)	1 (1.1)
37-72	75	52 (69.3)	18 (24)	4 (5.3)	1 (1.4)
>72	68	40 (58.8)	17 (25)	10 (14.7)	1 (1.5)

most children tested are located on the left side of the graph, drawing an abnormal distribution. Additionally, the distribution profile obtained using the WHO Child Growth Standards and the growth reference data[9, 10] confirms that these standards are not suitable for the anthropometric assessment of children with Down syndrome.

Discussion

This was a population of reasonably well-nourished lower and middle class children of the metropolitan area of Guadalajara (40.7% of the minimum wage in food expenditures per capita is equivalent to 1.9 US dollars per family member) and whose parents were people with average educational attainment for this setting (8.6 years). As has been shown in other studies[6, 12, 13], the growth of children with Down syndrome differs from the growth of healthy children. In Mexico, the WHO Child Growth Standards and the growth reference data[9, 10] have been adopted for assessing the growth and nutritional status of healthy children from birth to 19 years of age[14, 15]; however, to date, a reference standard for the growth and nutritional status of children with Down syndrome has not been identified.

The first comparison of children with DS with the US and Spanish reference patterns showed that the percentage of participants located below the 50th percentile in the height/age index was significantly higher using the pattern of Spanish reference in all of the age groups (0-36, 36-72 and> 72 months). However, when applying the test of goodness of fit, the US reference pattern also had a significant majority of children below the 50th percentile in the age groups of 0-36 months but not in the groups of 37-72 and older than 72 months of age. After that, age/height tended to normalize with no significant differences, unlike what we observed using the Spanish reference pattern in which most children remained below the 50th percentile in all age groups.

It could be speculated that the reason why the deficits in the age/height index tend to normalize in the age group older than 72 months in our population with the use of the US reference standard and not earlier could be that children with DS would have the best development in the US that would positively influence early life, such as differences in the severity of heart disease and/or whether surgical treatment was performed, and because school age children studied tend to normalize their growth.

Figure 1 clearly shows that the distribution of growth in Mexican children with DS was more similar to the US reference pattern[6], mainly from the 30th percentile, while the distribution was skewed to the left using the Spanish reference pattern[8]. When our population was compared with the WHO Child Growth Standards and the growth reference data[9, 10], the vast majority of children in the three age groups were below the 50th percentile. Over half were below the 3rd percentile, which would confirm that the WHO reference data are not adequate for assessing children with DS in different stages of growth.

Furthermore, it is noteworthy that only 20.8% of our population had a higher BMI above one standard deviation (13.6% overweight and 7.2% obese). In a study by the Netherlands Organisation for Applied Scientific Research Leiden, Van Gameren-Oosterom et al.[16] sta-

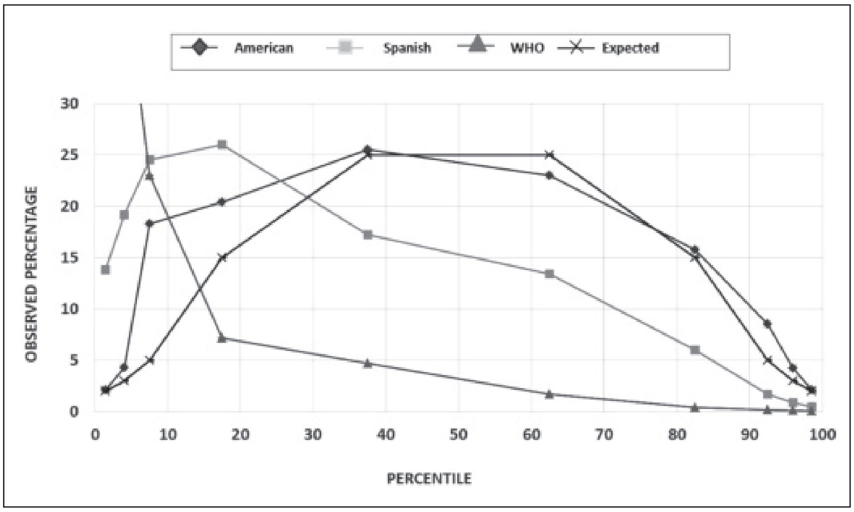

Fig. 1.—The percentile distribution of the observed frequency of the indicator height for age in Mexican children with Down syndrome according to the American, Spanish and WHO growth reference patterns.

tes that children with DS have twice the risk of obesity compared with other children. The study found that 57% of children with DS had a BMI diagnosed as overweight and 9.3% were obese, compared with children without DS among only 27% were overweight and 3.9% were obese. According to these researchers, possible physiological causes for this phenomenon include differences in metabolism and appetite control; unhealthy behavioral differences concerning motor skills that decrease physical activity and non-healthy lifestyles related to food. Matute et al[17] have shown that in Spain children and adolescents with Down syndrome (DS) are less active and with higher prevalence of overweight and obesity than those without DS but the information regarding physical activity (PA) in adolescents with DS is few and inconclusive. In addition, a study from Soler & Xandri[18] showed that obesity in adult with Down syndrome is a prevalent phenomenon.

One question that arose was why the Mexican children looked more like the American reference pattern than the Spanish reference pattern. One possibility is that the Spanish reference pattern excluded children with heart disease who have systemic repercussions, hypothyroidism and celiac disease, unlike the American reference pattern in which children with moderate and/or severe heart disease were included (although there were no references of hypothyroidism).

In our sample, 46% of children had some type of heart disease, and 56% of the heart disease cases were corrected. We should remember that in our study, at the time of evaluation, most children were healthy and/or their heart disease had been corrected; only 5.4% of heart disease had hemodynamic consequences. In addition, in our study, 9% of children had hypothyroidism; it has been noted that approximately 20% of children with DS have this disease[19]**.** It should also be noted that Cronk et al.[6] found that children with moderate and/or severe heart disease were 2 and 1.5 cm smaller size than children without heart disease or mild disease, respectively.

Worldwide, there are several reference patterns specific for the evaluation of children with DS: USA, Spain, Holland, Turkey, Egypt, the United Kingdom and Ireland, Portugal, Sicily, Arabia, Sweden[6, 7, 8, 13, 20-25]; and it has been observed that the growth profile of children with DS differs among countries, even among older age groups.

Tüyüs et al.[13] have noted that Swedish, English and Portuguese children with DS are taller than American and Sicilian children with DS, although these differences may be more or less noticeable according to age groups. Van Gameren-Oosterom et al.[21] found that the height of Dutch children with DS was greater than that of Americans. Therefore, anthropometric differences observed in children with DS impede the use of a single reference pattern to be adopted by all countries. Pinheiro et al.[4] compared 116 Chilean children with DS using with the American[6] and Spanish[8] reference patterns. They noted that there was poor agreement in the distribution obtained using the different standards and that the Spanish reference pattern was more similar to the Gaussian distribution curve in the weight/age and height/age indices. They concluded that the Spanish reference pattern better discriminates deficits and excesses.

In another study conducted in Brazil[26] among 90 children and 40 adolescents with DS, it was observed that with the weight/age index had a higher proportion of children below the 50th percentile using the Spanish reference and a higher proportion of children above the 95th percentile using the American reference pattern. The adolescent group had a higher proportion above the 95th percentile compared with the Spanish charts. Regarding the height/age index, there were a higher proportion of children below the 5th percentile compared with the Spanish reference pattern and no differences in the adolescent group were identified when comparing the two reference patterns.

Differences in the height of children with DS are observed among European countries. The selected sample likely contributes to these differences. For example, in the Netherlands[21], the children included came from their own reference pattern. First, they were categorized according to their health status, and only healthy children or those with mild heart disease were included; children with mosaicisms and translocations, prematurity, severe heart disease, other disorders and malformations affecting growth were excluded. Bertapelli et al.[27] conducted a systematic review of the different reference patterns for population with DS to verify eligibility and identified differences and similarities between studies. It is evident from the results that studies need to develop new specific references for children with DS that are reproducible at national and international levels. The main limitations of our study were that the number of participants was small and that the data cannot be extrapolated to the whole country.

Conclusions

The WHO Child Growth Standards and the growth reference data (2006, 2007) are not suitable for the anthropometric assessment of children with Down syndrome. The American reference pattern better fits the growth of Mexican children with DS than the Spanish reference pattern. It is necessary to develop new studies with a representative sample of children with DS in Mexico in order, to develop a Mexican reference pattern for children with DS that allows for an accurate assessment of their nutritional status and growth across age groups from birth to the pubertal stage.

Competing interests

The authors have declared that no competing interests exist.

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