

Body Composition in Children And Adolescents With Down Syndrome: Sex Differences and Associated Clinical Comorbidities

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Abstract:

Background: Children with Down syndrome (DS) have specific body composition patterns, characterized by differences in adiposity and muscle mass. Using anthropometric measurements cannot provide accurate information about these differences. Bioelectrical impedance analysis (BIA) gives a practical, non-invasive method for estimation of body composition; but, its accuracy depends on the used device, prediction equations, and characteristics of the population assessed [1,2].

Aim: we aim to describe body composition measurements using bioimpedance analysis in children and adolescents with DS and to clarify differences in sex, congenital heart disease, and hypothyroidism.

Subjects and Methods: This study included 206 children and adolescents with DS who had at least one recorded BIA measurement. Total fat mass, total body fat percentage, trunk fat mass and trunk fat percentage, are included in body composition parameters assessment. Muscle mass was registered as a predicted value obtained from the BIA assessment. Body composition measurements were examined and analyzed based on sex, cardiac condition, and hypothyroidism status

Results: The mean age at BIA assessment was 10.5 ± 3.3 years. The mean total fat mass was 8.2 ± 7.1 kg, while the mean total body fat percentage was $19.5 \pm 8.0\%$. Mean trunk fat mass and trunk fat percentage were 3.1 ± 3.1 kg and $13.5 \pm 7.9\%$, respectively. Mean predicted muscle mass was 16.0 ± 6.0 kg. Females had a higher mean total body fat percentage than males ($21.5 \pm 8.0\%$ versus $18.2 \pm 7.8\%$), whereas males had a higher mean predicted muscle mass (16.5 ± 6.3 versus 15.3 ± 5.6 kg). Children with cardiac disease had lower mean absolute fat mass and predicted muscle mass than those without cardiac disease, while mean total body fat percentages were similar. Body composition measurements were broadly similar between children with and without hypothyroidism.

Conclusion: The results show descriptive differences in body composition measurements through BIA according to sex and cardiac condition in children and adolescents with DS. These results indicate standardised measurement protocols for better assessment and accurate evaluation of body composition.

List of Abbreviations

BIA Bioelectrical Impedance Analysis
 BMI Body Mass Index
 DS Down Syndrome
 DXA Dual-Energy X-ray Absorptiometry
 CHD Congenital Heart Disease
 SD Standard Deviation
 Q1 First Quartile
 Q3 Third Quartile
 N Total number of participants
 kg Kilogram
 cm Centimeter

Introduction:

Down syndrome (DS) is the most common chromosomal disorder and genetic etiology of intellectual disability in humans, with the incidence rates of approximately 1/750 to 800 live births worldwide [13]. Down syndrome is caused by an extra 21 chromosome, presenting with unique facial features, such as a small and flat head with flat nasal bridge, up-slanted eyes, small mouth, small ears, and short neck. Generally, children with DS are associated with multiple congenital anomalies including cardiovascular, gastrointestinal, endocrine, and/or neuromuscular and growth and development impairment. So individuals with down syndrome have characteristic

patterns of growth and development, and risk of several medical and nutritional complications[14]. Assessment of nutritional status in children with DS is particularly important because conventional anthropometric measurements, including weight, height and body mass index (BMI), do not directly distinguish between fat mass and fat-free mass. So, body composition assessment can provide more information about nutritional status more than that obtained from anthropometric measurements alone [1,3]. Children and adolescents with DS may exhibit differences in adiposity and body composition compared with normal developing individuals. However, assessment of the body fat and classification of overweight and obesity may vary according to the assessment method. O'Shea et al and Machado et al demonstrated differences in the prevalence of obesity when BMI-based criteria were compared with body fat percentage estimated using BIA in children and young people with DS [3-4]. Bioelectrical impedance analysis is a non-invasive technique that evaluate the body composition from the electrical characters of biological tissues. BIA determines the total fat mass, percentage body fat, regional adiposity, and predicted muscle parameters. Hydration status, age, body size, measurement conditions, and the equations incorporated into the device affect the results. Therefore, the selection of appropriate population-specific and device-specific equations is very important when interpreting BIA-derived measurements [1,2]. The importance of body composition assessment in DS isn't only in the identification of adiposity. Body composition and laboratory parameters in children with DS were evaluated and associations between adiposity measurements and selected metabolic markers were reported [5] Emphasizing on the value of examining body composition in evaluating the metabolic health of children with DS. Presence of associated comorbidities should be considered in evaluating body composition in down syndrome children and adolescents. Presence of cardiac anomalies strongly affect growth and nutritional status, and also hypothyroidism associated with poor weight regulation and reduced linear growth. By examining total and trunk adiposity with predicted muscle mass, this study aims to provide additional descriptive data on body composition in down syndrome population and to explore the clinical importance of BIA in pediatric nutritional assessment.

Study design and participants:

The study included 206 children and adolescents with Down syndrome who had at least one recorded bioelectrical impedance assessment. The available data were analyzed to characterize body composition and explore differences according to sex, cardiac condition, and hypothyroidism status. The mean age at the time of bioelectrical impedance assessment was 10.5 ± 3.3 years. The study population comprised 127 males and 79 females. Body composition was assessed using bioelectrical impedance analysis (BIA) using Tanita BC-418MA body composition analyzer (Tanita Corp., Tokyo, Japan) according to the manufacturer's instructions. Measurements were obtained on the morning of the study after an overnight fast and after the subject had voided. The subject stood on the two foot plates with legs apart catching the two hand electrodes for one minute. It provides measurements for total and segmental body composition [12]. The recorded variables included total fat mass, total body fat percentage, trunk fat mass, trunk fat percentage, and predicted muscle mass. Total fat mass and trunk fat mass were expressed in kilograms, whereas total body fat and trunk fat percentages were expressed as percentages. Muscle mass was recorded as a predicted value derived from the BIA assessment. Body composition measurements were examined according to sex, cardiac condition, and hypothyroidism status. Cardiac condition and Hypothyroidism statu was categorized as present or absent.

Results:

Bioimpedance measurements were available for 206 children with Down syndrome, including 127 males and 79 females. The mean age at the time of bioimpedance assessment was 10.5 ± 3.3 years, with a median age of 10.0 years (Q1–Q3: 8.0–13.0 years). The mean total fat mass was 8.2 ± 7.1 kg, with a median of 5.9 kg (Q1–Q3: 3.3–10.9 kg). The mean percentage of total body fat was $19.5 \pm 8.0\%$, with a median of 17.5% (Q1–Q3: 13.2–24.5%). Trunk fat mass had a mean of 3.1 ± 3.1 kg and a median of 2.1 kg (Q1–Q3: 1.0–4.4 kg), while trunk fat percentage had a mean of $13.5 \pm 7.9\%$ and a median of 11.6% (Q1–Q3: 7.4–19.3%). The mean predicted muscle mass was 16.0 ± 6.0 kg, with a median of 14.9 kg (Q1–Q3: 11.2–20.1 kg).

The mean age at bioimpedance assessment was similar between males and females, being 10.5 ± 3.3 years in males and 10.4 ± 3.4 years in females. Females had a higher mean total fat mass than males (8.8 ± 7.1 vs. 7.8 ± 7.1 kg), with corresponding median values of 6.7 and 5.8 kg, respectively. Similarly, the mean percentage of total body

fat was higher among females than males ($21.5 \pm 8.0\%$ vs. $18.2 \pm 7.8\%$), with median values of 18.6% and 16.7%, respectively. Trunk fat mass was broadly comparable between the two sexes, with mean values of 3.2 ± 3.1 kg in females and 3.1 ± 3.1 kg in males. Trunk fat percentage was also relatively similar, although slightly higher among females ($14.0 \pm 8.3\%$) compared with males ($13.2 \pm 7.7\%$). In contrast, predicted muscle mass was higher among males, with a mean of 16.5 ± 6.3 kg compared with 15.3 ± 5.6 kg among females. The corresponding median values were 15.1 kg and 14.2 kg, respectively. Overall, the descriptive findings demonstrated a pattern of greater adiposity measures among females and greater predicted muscle mass among males in this bioimpedance subgroup (Table 1).

Table (1) : Bioimpedance data by sex in children with at least one bioimpedance measurement (N = 206).

Variable	Overall N = 206	Male N = 127	Female N = 79
Age at bioimpedance assessment (years)			
Mean (SD)	10.5 (3.3)	10.5 (3.3)	10.4 (3.4)
Median (Q1, Q3)	10.0 (8.0, 13.0)	10.0 (8.0, 13.0)	10.0 (8.0, 13.0)
Total fat mass			
Mean (SD)	8.2 (7.1)	7.8 (7.1)	8.8 (7.1)
Median (Q1, Q3)	5.9 (3.3, 10.9)	5.8 (3.0, 10.1)	6.7 (3.8, 12.2)
Total fat (%)			
Mean (SD)	19.5 (8.0)	18.2 (7.8)	21.5 (8.0)
Median (Q1, Q3)	17.5 (13.2, 24.5)	16.7 (12.2, 23.2)	18.6 (15.0, 27.6)
Trunk fat mass			
Mean (SD)	3.1 (3.1)	3.1 (3.1)	3.2 (3.1)
Median (Q1, Q3)	2.1 (1.0, 4.4)	2.1 (1.0, 4.1)	2.3 (0.9, 4.6)
Trunk fat (%)			
Mean (SD)	13.5 (7.9)	13.2 (7.7)	14.0 (8.3)
Median (Q1, Q3)	11.6 (7.4, 19.3)	11.6 (7.5, 18.6)	12.3 (7.0, 20.3)
Predicted muscle mass			
Mean (SD)	16.0 (6.0)	16.5 (6.3)	15.3 (5.6)
Median (Q1, Q3)	14.9 (11.2, 20.1)	15.1 (11.5, 20.3)	14.2 (10.9, 19.8)

When the bioimpedance parameters were examined according to the presence of a cardiac condition, 159 children had no documented cardiac condition and 47 had a cardiac condition. The proportion of males was higher among children without a cardiac condition (66.0%), whereas females represented a slightly greater proportion of the cardiac-condition group (53.2%). The mean age at bioimpedance assessment was 10.7 ± 3.4 years in children without a cardiac condition and 9.8 ± 2.9 years among those with a cardiac condition. Children without a cardiac condition had a higher mean total fat mass (8.4 ± 7.5 kg) compared with those with a cardiac condition (7.3 ± 5.4 kg). However, the mean percentage of total body fat was very similar between the two groups ($19.4 \pm 8.1\%$ and $19.6 \pm 7.8\%$, respectively). The median percentage of total body fat was also comparable, at 17.5% in children without cardiac disease and 17.6% in those with cardiac disease. A similar pattern was observed for trunk fat mass, with a mean of 3.3 ± 3.3 kg in children without a cardiac condition compared with 2.7 ± 2.4 kg in those with a cardiac condition. Trunk fat percentage showed relatively close mean values between the groups ($13.6 \pm 8.0\%$ vs. $13.1 \pm 7.6\%$, respectively). Predicted muscle mass was higher in children without a cardiac condition, with a mean of 16.5 ± 6.2 kg compared with 14.5 ± 5.3 kg among those with a cardiac condition. The corresponding median values were 15.5 kg and 13.5 kg, respectively. (Table 2)

Table (2): Bioimpedance data by cardiac condition in children with at least one bioimpedance measurement (N = 206).

Variable	No N = 1591	Yes N = 471
Sex		
Male	105 (66.0%)	22 (46.8%)

Female	54 (34.0%)	25 (53.2%)
Age at bioimpedance assessment (years)		
Mean (SD)	10.7 (3.4)	9.8 (2.9)
Median (Q1, Q3)	10.0 (8.0, 13.0)	10.0 (8.0, 11.0)
Total fat mass		
Mean (SD)	8.4 (7.5)	7.3 (5.4)
Median (Q1, Q3)	6.2 (3.4, 10.4)	5.0 (3.1, 12.6)
Total fat (%)		
Mean (SD)	19.4 (8.1)	19.6 (7.8)
Median (Q1, Q3)	17.5 (13.2, 24.6)	17.6 (13.3, 24.4)
Trunk fat mass		
Mean (SD)	3.3 (3.3)	2.7 (2.4)
Median (Q1, Q3)	2.1 (1.0, 4.5)	1.5 (0.9, 4.4)
Trunk fat (%)		
Mean (SD)	13.6 (8.0)	13.1 (7.6)
Median (Q1, Q3)	11.9 (7.0, 19.8)	11.6 (7.5, 17.8)
Predicted muscle mass		
Mean (SD)	16.5 (6.2)	14.5 (5.3)
Median (Q1, Q3)	15.5 (11.3, 20.5)	13.5 (10.5, 17.1)
1n (%)		

According to thyroid status, 55 children had no documented hypothyroidism and 151 had hypothyroidism. Males constituted 67.3% of the children without hypothyroidism and 59.6% of those with hypothyroidism, while females represented 32.7% and 40.4%, respectively. The mean age at bioimpedance assessment was 10.0 ± 3.5 years among children without hypothyroidism and 10.6 ± 3.2 years among those with hypothyroidism. The mean total fat mass was similar between children without and with hypothyroidism (8.0 ± 8.0 kg and 8.2 ± 6.7 kg, respectively). Likewise, mean total body fat percentage was almost identical in the two groups, at $19.5 \pm 7.8\%$ and $19.4 \pm 8.1\%$, respectively. Median total body fat percentages were also comparable (17.4% and 17.6%). Trunk fat mass showed similar mean values in children without and with hypothyroidism (3.2 ± 3.3 kg and 3.1 ± 3.0 kg, respectively), while mean trunk fat percentage was $13.8 \pm 7.7\%$ and $13.4 \pm 8.0\%$, respectively. Predicted muscle mass was also broadly comparable, with mean values of 15.9 ± 6.6 kg in children without hypothyroidism and 16.1 ± 5.8 kg in those with hypothyroidism. The corresponding median values were 13.9 kg and 15.2 kg.

Table (3): Bioimpedance data by hypothyroidism in children with at least one bioimpedance measurement (N = 206).

Variable	No N = 551	Yes N = 1511
Sex		
Male	37 (67.3%)	90 (59.6%)
Female	18 (32.7%)	61 (40.4%)
Age at bioimpedance assessment (years)		
Mean (SD)	10.0 (3.5)	10.6 (3.2)
Median (Q1, Q3)	10.0 (7.0, 13.0)	10.0 (8.0, 13.0)
Total fat mass		
Mean (SD)	8.0 (8.0)	8.2 (6.7)
Median (Q1, Q3)	5.7 (2.7, 9.1)	6.0 (3.4, 11.4)
Total fat (%)		
Mean (SD)	19.5 (7.8)	19.4 (8.1)
Median (Q1, Q3)	17.4 (13.3, 25.0)	17.6 (13.2, 24.4)
Trunk fat mass		
Mean (SD)	3.2 (3.3)	3.1 (3.0)
Median (Q1, Q3)	2.2 (1.1, 4.0)	2.0 (0.9, 4.5)

Trunk fat (%)		
Mean (SD)	13.8 (7.7)	13.4 (8.0)
Median (Q1, Q3)	11.6 (7.6, 20.0)	11.6 (6.9, 18.9)
Predicted muscle mass		
Mean (SD)	15.9 (6.6)	16.1 (5.8)
Median (Q1, Q3)	13.9 (10.5, 20.0)	15.2 (11.2, 20.3)
1n (%)		

Statistical Analysis:

Statistical analysis was performed using R (RC Team. (2020)). Categorical data were presented as frequencies and percentages, whereas continuous data were presented as means and standard deviations (SD) and medians with the 25th and 75th percentiles[15].

Discussion:

The mean total fat mass in the present study was 8.2 ± 7.1 kg, while the mean total body fat percentage was $19.5 \pm 8.0\%$. Mean trunk fat mass was 3.1 ± 3.1 kg, and mean trunk fat percentage was $13.5 \pm 7.9\%$. The mean predicted muscle mass was 16.0 ± 6.0 kg. The relatively wide standard deviations results indicate variation in estimation of body composition measurements within the study population mostly due to down syndrome children difference in age, body size, developmental stage, physical activity, nutritional status, and associated comorbidities. So, a single mean value cannot be used in evaluating the body composition of every child with DS. body fat percentage using BIA and dual-energy X-ray absorptiometry (DXA) in 70 children with DS was assessed by Loveday et al. [1] and reported that mean body fat percentages of 30.5% in females and 22.5% in males and emphasized the strong correlations between BIA-derived and DXA-derived body fat percentages supporting the potential importance of BIA for estimating adiposity in down syndrome children. A correlation between BIA and DXA does not necessarily establish close agreement between the two methods for individual participants. The accuracy of BIA-derived variables depends on the observed data used and the characteristics of the population being assessed [1,2]. Machado et al. [3] also investigated body composition using BIA in children and adolescents with DS, providing added evidence that this technique has been applied to nutritional assessment in this population. One of the principal clinical considerations in the nutritional assessment of children with DS is that BMI and body composition describe related but distinct characteristics. BMI is calculated from body weight and height and is commonly used to screen for overweight and obesity. But, it cannot distinguish between fat mass and fat-free mass, and cannot assess the fat distribution. Hatch-Stein et al. [4] examined body composition and developed BMI growth charts for children with DS, highlighting the importance of considering body composition when evaluating weight in this population. Similarly, O'Shea et al. [5] studied overweight and obesity in 61 children and young people with DS aged 4–16 years using BMI and BIA-derived body fat percentage. Using the International Obesity Task Force BMI cut-offs, the authors classified 51.6% of males and 40.0% of females as overweight or obese, compared with 32.0% of males and 14.8% of females when classification was based on body fat percentage. Mean BIA-derived body fat percentage was higher in females than in males, at 22.38% and 18.76%, respectively. The differences between BMI-based and body-fat-based classifications illustrate that the two approaches do not identify the same individuals to have excess adiposity [5].

The higher mean total body fat percentage in females is consistent with the sex-related difference reported by Loveday et al. [1]. O'Shea et al. [5] likewise reported a higher mean body fat percentage in females than in males in their study population. The consistency in the direction of these observations suggests that sex is an important variable to consider when interpreting body composition in this population. Talma et al. [6] reviewed the validity, reliability, responsiveness, and measurement error of BIA in children and adolescents. Their review highlighted limitations in criterion validity and measurement error. Orsso et al. [2] discussed the methodological issues involved in using BIA in children and adolescents, including the importance of appropriate prediction equations and standardized measurement conditions. Children with cardiac disease had a lower mean total fat mass than those without recorded cardiac disease (7.3 ± 5.4 versus 8.4 ± 7.5 kg). Mean trunk fat mass was also lower in the cardiac disease group (2.7 ± 2.4 versus 3.3 ± 3.3 kg). Mean predicted muscle mass was 14.5 ± 5.3 kg in children with cardiac disease and 16.5 ± 6.2 kg in those without cardiac disease. In contrary to, mean total body fat

percentage was identical between the groups, at $19.6 \pm 7.8\%$ and $19.4 \pm 8.1\%$, respectively. Mean trunk fat percentage was also comparable, measuring $13.1 \pm 7.6\%$ in the cardiac disease group and $13.6 \pm 8.0\%$ in the group without cardiac disease. This pattern illustrates an important distinction between absolute body composition measurements and percentages. Absolute fat mass is expressed in kilograms and is influenced by overall body size. Body fat percentage expresses estimated fat mass relative to total body weight. So, lower absolute fat mass can coexist with a similar body fat percentage when overall body weight differs between groups. The lower mean predicted muscle mass in children with cardiac disease requires close interpretation. The cardiac disease group was younger on average than the group without cardiac disease (9.8 ± 2.9 versus 10.7 ± 3.4 years) and had a different sex distribution. In the cardiac disease group, 46.8% of participants were male, compared with 66.0% in the group without cardiac disease. These differences could contribute to the observed variation in absolute body composition measurements. The relationship between thyroid function and body composition is likely to depend on the clinical definition of hypothyroidism, the severity and duration of thyroid dysfunction, biochemical control, and treatment status. Individuals with hypothyroidism who are untreated or inadequately controlled disease should be differed from those receiving appropriate therapy and tested for thyroid function that shows normal results [10-11]. Hydration status, age, body size, measurement conditions, and the equations incorporated into the device affect the results. The relative importance of these factors depends on the device accuracy and the population characters being assessed [2,7,8]. The degree of standardization in BIA studies and the need for accurate measurement protocols are described by Brantlov et al. [8]. As growth and changes in body proportions can affect the relationships between impedance measurements and body composition, these considerations are of great importance in children.

Clinical implications

It is very important to evaluate multiple body composition parameters in children and adolescents with DS. Total fat mass, total body fat percentage, trunk fat measurements, and predicted muscle mass give added information and help to assess the nutritional status more than using the body weight alone. Children with cardiac disease had lower mean absolute fat mass than those without cardiac disease, but, the mean total body fat percentages were similar in both groups. However, the present study does not establish that BIA is superior to BMI or that it can independently diagnose obesity, malnutrition, or low muscle mass in children with DS. Its clinical usefulness depends on the accuracy of the device estimates and the availability of appropriate standards [1,2,6].

Strengths

- Incorporation of BIA provides information beyond conventional anthropometric measurements, including fat mass, body fat percentage, and predicted muscle mass.
- Assessment of body composition in a relatively substantial subgroup of children with Down syndrome.
- Evaluation of sex-related differences in body composition parameters.
- Assessment of associated comorbidities: Exploration of differences in body composition according to the presence of congenital heart disease and hypothyroidism.
- Assessment of total and regional adiposity, including trunk fat mass and trunk fat percentage.

Limitations:

- BIA allows indirect method for estimation of body composition
- Measurement accuracy is affected by Age and hydration status.
- Predicted muscle mass isn't representative to skeletal muscle mass.

Conclusion

The findings show descriptive differences in body composition measurements obtained by BIA based on sex and cardiac condition in children and adolescents with DS. Males had a higher mean predicted muscle mass, but females had a higher mean total body fat percentage. Children who have cardiac disease had relative lower mean absolute fat mass and predicted muscle mass, inspite of similar mean total body fat percentages. These findings

recommend standardized measurement protocols for better assessment and accurate evaluation of body composition.

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