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Original article

Estimation of percent body fat based on anthropometric measurements in children and adolescents with congenital adrenal hyperplasia due to 21-hydroxylase deficiency

Ezequiel M. Gonçalves [a,b,*], Analiza M. Silva [c], Catarina N. Matias [c], Sofia H.V. Lemos-Marini [d], Allan O. Santos [e], Gil Guerra-Júnior [a,d]

[a] Growth and Body Composition Laboratory, Center for Investigation in Pediatrics (CIPED), Faculty of Medical Sciences (FCM), State University of Campinas (UNICAMP), Campinas, SP, Brazil
[b] Post-graduate Program for Child and Adolescent Health, FCM – UNICAMP, Campinas, SP, Brazil
[c] Exercise and Health Laboratory, Faculty of Human Kinetics, Technical University of Lisbon, Estrada da Costa, 1495-688 Cruz-Quebrada, Portugal
[d] Department of Pediatrics, Pediatric Endocrinology Unit, FCM – UNICAMP, Campinas, SP, Brazil
[e] Division of Nuclear Medicine, Clinical Hospital, UNICAMP, Campinas, SP, Brazil

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S U M M A R Y

Background & aim: Congenital adrenal hyperplasia due to 21-hydroxylase deficiency is associated with a high risk for obesity. Anthropometric measures are simple and inexpensive methods to assess body fat. However, the accuracy of alternative methods in these patients is unknown. This study aim to develop and evaluate the accuracy of predictive anthropometric equations in the estimation of percent body fat in individuals with congenital adrenal hyperplasia due to 21-hydroxylase deficiency.
Methods: A total of 31 female and 22 male patients, aged 7–20 years, were evaluated. Dual-energy X-ray absorptiometry was used as the reference method for body fat, and anthropometric measurements were performed.
Results: Three new predictive equations showed similar results: Equation (1) ($R^2 = 0.85$; SEE = 2.89%), Equation (2) ($R^2 = 0.86$; SEE = 2.82%), and Equation (3) ($R^2 = 0.86$; SEE = 2.81%). Internal cross-validation procedures showed a high R^2 (range, 0.84–0.85) and low SEE (<3%). The limits of agreement ranged from −5.6% to 5.6% and no trend was observed.
Conclusion: In children and adolescents with congenital adrenal hyperplasia due to 21-hydroxylase deficiency, three new predictive equations were validated for the estimation of percent body fat, with dual-energy X-ray absorptiometry as the reference method.

1. Introduction

Congenital Adrenal Hyperplasia (CAH) represents a group of diseases characterized by the deficiency of one of the enzymes responsible for cortisol biosynthesis.[1,2] The most common impairment of CAH is the deficiency of the 21-hydroxylase enzyme (CAH-21OHD), accounting for more than 90% of cases. The disease results in low production of glucocorticoids and excess androgens, with or without mineralocorticoid insufficiency.[1] Congenital adrenal hyperplasia due to 21-hydroxylase deficiency (CAH-21OHD) is a common genetic endocrine disorder.[1,3] The classic form of CAH-21OHD has an incidence of 1:15,000 live births and diverges according to ethnicity and country.[1,2,4] High rate was reported in Brazil, about 1:10,325 live births.[5] Inadequate therapy may cause early puberty, short stature and infertility due to androgen excess (hyperandrogenism) while a high dose treatment may cause insulin resistance, osteoporosis and increased body fat due to the effects of hypercortisolism.[6–9]

Body fat assessment is an important tool in the evaluation of nutritional status and monitoring the treatment of individuals with CAH, mainly because these patients present higher risk of

Abbreviations: CAH, congenital adrenal hyperplasia; CAH-21OHD, congenital adrenal hyperplasia due to 21-hydroxylase deficiency; %BF, body fat; DXA, dual-energy X-ray absorptiometry; SKF, skinfolds.

* Corresponding author. Growth and Body Composition Laboratory, Center for Investigation in Pediatrics (CIPED), Faculty of Medical Sciences (FCM), State University of Campinas (UNICAMP), Campinas, SP, Brazil. Tel.: +55 19 35217353; fax: +55 19 3521 7322.

E-mail addresses: ezequiel@fcm.unicamp.br, emaildozeique@gmail.com (E.M. Gonçalves), analiza@fmh.utl.pt (A.M. Silva), cmatias@fmh.utl.pt (C.N. Matias), sofia@hc.unicamp.br (S.H.V. Lemos-Marini), allanoliveirasantos@uol.com.br (A.O. Santos), gilguer@fcm.unicamp.br (G. Guerra-Júnior).

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obesity.[10,11] Several methods have been used to assess body composition in children and adolescents. Dual-energy X-ray absorptiometry (DXA) has emerged as one of the most widely accepted methods in the assessment of body composition, and is considered a valid and reliable method for assessing body composition in children and adolescents,[12,13] however this assessment involves extended laboratory facilities. Consequently, it is important to identify alternative methods that are convenient, reliable and accurate in measuring body composition in this special population. Anthropometry may provide an alternative as it is a simple, noninvasive, and inexpensive method, especially when compared with other laboratory-based methods. However, it is difficult to find the appropriate balance in glucocorticoid replacement therapy, which can compromise the accuracy and applicability of this method in patients with CAH, once these patients may present changes in body fat due to the effects of glucocorticoid therapy, or greater lean mass reflecting the adverse effects of prolonged androgen exposure.[9]

Models based on anthropometric measurements are widely used to predict total body fat in children and adolescents, but these are generally based on samples of healthy individuals.[12–15] To our knowledge, a predictive equation based on anthropometric measurements for CAH patients does not exist, and its accuracy has not yet been determined in this population.

Therefore, the aim of the present investigation was to develop and evaluate the accuracy of percent body fat (%BF) predictive equations based on anthropometric measurements in individuals with classic CAH-21OHD using dual-energy X-ray absorptiometry (DXA) as the reference method.

2. Materials and methods

2.1. Subjects

A total of 53 patients (31 females and 22 males), aged 7–20 years were evaluated. All of the patients were diagnosed with classic CAH due to 21-hydroxylase deficiency (21OHD) confirmed by clinical, hormonal, and molecular analyses. Of the total, sixteen subjects were diagnosed with the simple-virilizing (SV) form, and 38 were diagnosed with the salt-wasting (SW) form. All of the patients were diagnosed and followed in the Outpatient Pediatric Endocrinology Clinic of the Clinical Hospital, State University of Campinas (UNICAMP), Brazil. Pubertal development was classified according to Marshall and Tanner[16,17] criteria, by a single pediatric endocrinologist. All measurements were carried out in the same day while the patients visited the outpatient clinic. All subjects and parents or tutors were informed about the possible risks of the investigation before giving their written informed consent to participate. All procedures were approved by the Research Ethics Committee of UNICAMP and conducted in accordance to the declaration of Helsinki for human studies of the World Medical Associations.[18] In brief, the procedures are described below.

2.2. Glucocorticoid replacement

The patients received glucocorticoid replacement with hydrocortisone ($n = 36$), prednisone ($n = 6$), dexamethasone ($n = 7$) or a combination of hydrocortisone plus dexamethasone ($n = 4$). For the data analysis, the doses of the various glucocorticoids were converted using a growth-retarding cortisol equivalent (GRCE) formula: 80 mg hydrocortisone = 16 mg prednisone = 1 mg dexamethasone.[19] Forty-five patients (38 SW and 7 SV) additionally received fludrocortisones (FC) twice a day.

2.3. Anthropometry

Anthropometric measurements were performed using standardized procedures and conditions.[20] The measurements were performed by a highly trained technician in standardized conditions. Skinfolds (SKF) were measured three times to the nearest 0.1 mm and averaged for analysis. All SKF measurements (triceps, medial calf, subscapular, biceps, and suprailiac) were made on the right site of the body, according to the standardized anatomic locations and methods,[20] using a Lange caliper (Cambridge Scientific Instruments, Cambridge, MA). These data were used to calculate body mass index (BMI; kg/m^2), the sitting height/waist circumference ratio (SH/WC), sum of triceps and biceps SKF, sum of triceps and subscapular SKF, sum of triceps and medial calf SKF and sum of triceps, biceps, subscapular and suprailiac SKF. The BMI was used to classify the patients into normal, overweight, and obese according to age- and sex-specific cutoff points proposed by the International Obesity Task Force (IOTF).[21] On the basis of test–retest reliability using eight subjects, the technical error of measurement (TEM) for the anthropometric measurements ranged from 1.3% to 3.8%.

2.4. Dual-energy X-ray absorptiometry (DXA)

To assess %BF, DXA measurements were made with a whole-body scan on a fan beam Hologic model Discovery Wi densitometer, software version 12.7 (Hologic, Bedford, MA). According to the procedures recommended by the manufacturer, the densitometer was calibrated daily using a step phantom with six fields of acrylic and aluminum of varying thickness and known absorptive properties was scanned alongside each subject to serve as an external standard for the analysis of different tissue components. The same laboratory technician positioned the subjects, performed the scans and executed the analysis according to the operator's manual using the standard analysis protocol. Based on test–retest, the TEM was 0.498% for %BF, and the coefficient of variation was 1.32%, in our laboratory.

2.5. Statistical analysis

For the statistical analyses, SPSS (Statistical Package for the Social Sciences, Chicago, IL, USA) version 18.0 was used. The normal distribution of the data was tested using the Shapiro–Wilk test. Independent-sample *t*-tests were used to compare variables between genders, and Mann–Whitney *U* tests were used as the alternative if the data did not present a normal distribution. Scatter plots and Pearson's correlation coefficient were used to assess whether the relationship between the values of each independent variable (predictor) and dependent variable (% BF) demonstrated linearity. Stepwise regression analysis was performed to identify which combination of variables would best predict %BF measured by DXA. The adjusted coefficient of determination (R^2) and SEE were estimated. A variance inflation factor for each independent variable was also calculated to evaluate multicollinearity. Simple regression analysis was performed to determine the relationships between %BF predicted by the new equations and %BF assessed by DXA. Slopes and intercepts were examined. The adequacy of the final prediction models was assessed by testing the normality of the residuals and the correlation of the absolute residuals with the variables in the models. Differences between the reference method (DXA) and each new predictive equation were calculated using paired-sample *t*-tests. Agreement between the predictive equations and reference method was assessed using the Bland–Altman method.[22] The three models were then internally cross-validated in all of the models using the predicted residual sum of squares (PRESS) statistics method.[23] The PRESS statistic is obtained by (1) fitting a regression equation with one observation excluded, (2)