GETTING TO THE HEIGHT OF THE MATTER: THE RELATIONSHIP BETWEEN STATURE AND ADIPOSITY IN PRE-PUBERTAL CHILDREN

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Objective: Height has been inversely associated with cardiometabolic disease, with adiposity as the proposed contributor. Childhood represents a time when underlying metabolic pathways converge to determine growth. Although the extent to which influence is relevant, insulin, as a key growth signaling factor, likely provides key insight into mechanisms linking height and adiposity. Insulin concentration displays well-established sex and racial differences, with hyperinsulinemia more common among African Americans (AA) females relative to European Americans (EA). The objective of our study was to evaluate the relationship between height and adiposity in children. In addition, a secondary objective was to evaluate potential moderation by insulin concentration.

Design: Seventy-two pre-pubertal children aged 4–10 years (μ=6.6 ± .2) participated.

Main Outcome Measures: Percent fat was assessed by DXA and fasting insulin by serum assay.

Results: Height was positively associated with percent fat in the overall sample (P=.04). When evaluated according to age, an association was identified at age seven years (P=.02). When evaluated by sex, a positive relationship was apparent only in AA girls (P=.05). Inclusion of insulin in the model attenuated all significant associations, barring marginal significance in those aged seven years (P=.08).

Conclusions: A positive relationship between height and adiposity is apparent, particularly among those in younger years, which is contrary to what has been consistently reported in adults. Interestingly, age seven years was identified as a point of race-associated divergence in body composition. The degree to which growth-related processes in childhood underlie developmental origins of health disparities warrants further study. (*Ethn Dis.* 2013;23[1]:71–76)

Key Words: Height, Adiposity, Growth, Racial Disparities, Insulin

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INTRODUCTION

Numerous studies conducted in adults have established an inverse association between height and the prevalence of cardiometabolic diseases, which appears to be connected with obesity status.[1–3] Historically, shorter adults have been observed to have greater adiposity and paralleled heightened prevalence of cardiovascular disease and type 2 diabetes relative to taller counterparts.[2,4–7] Speculatively, insulin resistance, more prevalent among shorter adults, has provided a link between adiposity and chronic disease risk. Albeit limited, investigations of the height-fat nexus in children, however, report greater adiposity in tall children relative to those who are shorter.[2,8–10] The underlying reason(s) for the opposed associations according to life stage is not sufficiently understood.

Indeed, beyond the documented increasing BMI observed over the past three decades across various life stages, recognizable changes on body composition, especially adipose tissue accrual, have been identified. The contemporary environment in which children interact is increasingly 'obesogenic,' which has manifested into altered metabolic pathways, particularly that involving insulin homeostasis. The metabolic consequences of excess adipose tissue accrual, and consequential dysregulated insulin dynamics, may provide some insight into how early life growth processes may underlie initiation and progression of metabolic diseases. As the pediatric population continues to be burdened by ever-present obesity prevalence, investigation of underlying growth-related determinants is warranted.

Attainment of maximal adult stature is contingent on an optimal physiologic environment. Beyond the clear direct role of reproductive hormones, pubertal onset through associated hormonal changes secondary to adiposity, is largely encompassed by permissive effects of adipocytokines, which interact with growth factors. Insulin action and metabolic response to insulin is of particular importance as a key signaling factor. At the cellular level, insulin provides the means by which nutrients are metabolized and circulating concentration largely reflects developmental requirements. Marked changes throughout pubertal maturation influence insulin dynamics,[11,12] thereby altering metabolic and growth-related processes. Circulating insulin levels, particularly during growth when tissues are highly sensitive to mitogenic exposures, may represent a link between stature and metabolic risk.

Numerous investigations have demonstrated similarities in body composition trajectory as well as metabolic control across the sexes and among racial groups prior to reproductive maturation. However, peri-pubertal changes in insulin dynamics are well-established to display differences across groups. We and others have reported greater puberty-related insulin resistance with an attenuated rebound to pre-pubertal levels among African Americans (AA). In addition, the timing and tempo of reproductive maturation is accelerated among AA.[12–14] Of note, rapid linear growth early in the life course underlies theoretical framework of the developmental origins of health and disease. Conceivably, dysregulated insulin concentration and peripheral insulin resistance may contribute to growth-related differences between European American (EA) and AA boys and girls. Given unequal distribution of cardiometabolic disease risk among EA

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Table 1. Sample characteristics (mean ± standard error)

	Total (*N*=72)	Normal (*n*=36)	Obese (*n*=36)[a]
Age	6.6 ± .2	6.1 ± .3[b]	7.2 ± .4
Height	47.9 ± .9	45.5 ± 1.0[b]	50.4 ± 1.2
% fat	31.1 ± .1	23.7 ± .4[b]	38.6 ± 1.2
Lean	19.7 ± 1.0	16.3 ± .7[b]	23.1 ± 1.6
BMC	992.9 ± 47.5	838.5 ± 43.8[b]	1147.4 ± 76.7
Insulin	7.2 ± .7	5.5 ± .7[b]	9.1 ± 1.3
Glucose	92.0 ± 1.2	93.0 ± 1.9[b]	90.9 ± 1.4

[a] Obesity status defined by percent fat >25% for boys, >30% for girls as assessed by DXA.
[b] Indicates significant difference between normal and obese children.

and AA, in conjunction with the conjectured association between height and adiposity, stature in childhood may provide insight into the race-related developmental origin of adult diseases. The objective of this study was to evaluate the relationship between height and adiposity among AA and EA children and investigate if fasting insulin contributes to the relationship.

METHODS

Our study represents an ongoing cohort comprising participants enrolled in a variety of clinical studies, including dietary and physical activity interventions, and other metabolic/physiologic studies conducted at University of Alabama at Birmingham (UAB). Our current investigation is limited to cross-sectional analyses of baseline data for participants who underwent DXA scans and venipuncture over the period of 2009–2011. The total sample included seventy-two children aged 4–10 years, with approximately one-third of the sample being male, 42% AA and half of which were obese. All procedures were approved by the UAB Institutional Review Board and informed consent and assent (where appropriate) was obtained.

Anthropometric Assessment

Height and weight were measured using a portable stadiometer and digital scale. Total body composition (percent body fat mass and bone mineral content) was measured by DXA using a GE Lunar Prodigy densitometer (GE LUNAR Radiation Corp., Madison, WI), using pediatric software (enCORE 2002 Version 6.10.029) for analyses, with the coefficient of variation (CV) for repeated measures of total body fat mass as 6.55%. Children were scanned in light clothing, while lying flat on their backs with arms at their sides.

Metabolic Assays

Glucose and insulin were obtained by venipuncture after an overnight fast and assayed in the UAB Metabolism Core Laboratory of the Department of Nutrition Sciences. Glucose was measured in 10 µl sera using an Ektachem DT II System (Johnson and Johnson Clinical Diagnostics, Rochester, NY). The mean intra- and inter-assay CV for glucose analysis in the Core Laboratory are .61% and 1.45%, respectively. Insulin was determined in duplicate 100 µl aliquots using double-antibody radioimmunoassays (RIA) (Linco Research Inc., St. Charles, MO). The insulin assay has a sensitivity of 3.35 µIU/ml in the Core Laboratory, and a mean intra- and inter-assay CV of 3.49% and 5.57%, respectively.

Statistics

Differences at baseline in descriptive characteristics between groups were examined by ANCOVA to allow for inclusion of confounding variables (age, sex and race) where appropriate. Mul-

tivariate linear regression (Model A) was used to analyze the relationship between height and percent fat. A second regression model (Model B) was analyzed with inclusion of fasting insulin as a covariate. In addition, subgroup analysis by age, sex, race and adiposity was conducted. Adiposity models used 25% body fat for boys and 30% body fat for girls as cut-offs separating normal and excess adiposity.[15–17] All data were analyzed using SAS 9.2 software.

RESULTS

Sample characteristics of the total group, and by sex, race and obesity status are shown in Tables 1 and 2. Girls on average were older, taller and had greater percent fat, lean mass, and bone mineral content (BMC) than boys. Girls also had greater fasting insulin concentrations than boys. Stratification by race revealed AA were taller and had greater body fat percentage, lean mass, BMC, and fasting insulin concentrations, while having lower fasting glucose concentrations relative to EA children; these characteristics were also greater in children having excess adiposity compared to normal adiposity. There was no difference in age between EA and AA participants; however, children with excess adiposity were older than normal adiposity counterparts. Figure 1 illustrates height, percent fat and insulin concentration by race and sex. There was no race-related difference in height or percent fat among boys. However,

Table 2. Sex- and race-specific characteristics (mean ± standard error)

	Boys (n=23)[a]	Girls (n=49)	EA (n=42)	AA (n=30)
Age	5.0 ± .2[b]	7.4 ± .3	6.7 ± .3	6.4 ± .4
Height	43.2 ± 1.0[b]	50.2 ± 1.0	47.1 ± 1.0[c]	49.1 ± 1.4
%Fat	27.1 ± 1.4[b]	33.0 ± 1.4	28.7 ± 1.1[c]	34.5 ± 1.9
Lean	15.1 ± .9[b]	21.8 ± 1.2	17.6 ± .9[c]	22.6 ± 1.9
BMC	755.9 ± 51.0[b]	1104.2 ± 59.5	918.6 ± 45.4[c]	1096.9 ± 92
Insulin	5.4 ± 1.0[b]	7.9 ± .9	6.2 ± .9[c]	9.0 ± 1.1
Glucose	91.6 ± 2.4	92.2 ± 1.4	93.2 ± 1.4[c]	89.9 ± 2.3

[a] No boys included over age 8.
[b] Indicates significant difference between boys and girls.
[c] indicates significant difference between European Americans (EA) and African Americans (AA).

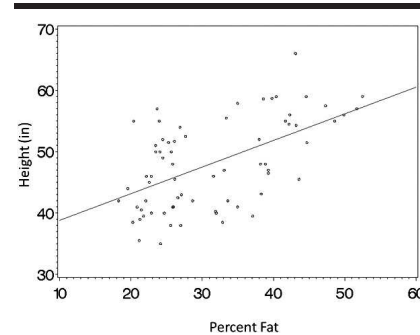Fig 2. Association between height and percent fat

AA girls were taller and had greater adiposity than EA girls. Further, AA boys had greater insulin concentration than EA boys.

Figure 2 illustrates the association between height and percent fat in the total sample. Multivariate regression analyses (Table 3) showed a significant positive relationship between height and percent fat ($P<.05$) in the total sample; however, when analyzed by age, only children aged 7 years maintained this significant association ($P=.02$). Inclusion of insulin in the model (Model B) attenuated the relationship ($P=.08$). When the regression analyses were stratified by race and sex (Table 4), a positive relationship between height and percent fat was found in AA ($P=.05$) and girls ($P=.05$) only, though the associations were attenuated by insulin. Additional stratification of race-specific models by sex indicated a positive

relationship between height and percent fat in AA girls ($P=.05$). Whereas analyses evaluating BMC and percent fat showed no racial difference among lean children, obese AA children had higher BMC ($P=.01$) than obese EA participants; however, the relationship was attenuated by insulin. When adjusting for height there were no significant differences among groups observed.

DISCUSSION

Although not a measure of health per se, height attainment in childhood may overlap biological pathways driving adiposity. Epidemiologic data has consistently reported an increasing prevalence of obesity in shorter adults.[2,3,7] On the contrary, we found a positive relationship of adiposity with height in

young children. This, along with findings from others reporting increased height in childhood with greater BMI as an adult,[8,9] suggests implications of growth patterns for long-term health. Although proximately adiposity may contribute to greater height, an associated deceleration of growth post-pubertally may be met with increasing adipogenic pathways, in addition to hindrance of maximal adult height. Further, rapid childhood growth has a host of physiologic and metabolic ramifications, many of which are not realized until later in life. Undoubtedly, the interrelationship between height and adiposity and the consequential effect of circulating growth factors (ie, insulin) represents an auspicious area of investigation when considering developmental origins of health, particularly in the context of disparities.

Variation in growth patterns seem to be embedded in our findings, specifically those encompassing sex and race. Sexual dimorphism in age of skeletal maturation onset is well known and characterized, with females approximately two years ahead of males, regarding both age at take-off and peak height velocity. Convincing evidence has also been found indicating higher body mass further advances pubertal progression,[18] as well as related growth processes. African Americans, through multiple metabolic pathways, may have heightened sensitivity in terms of devel-
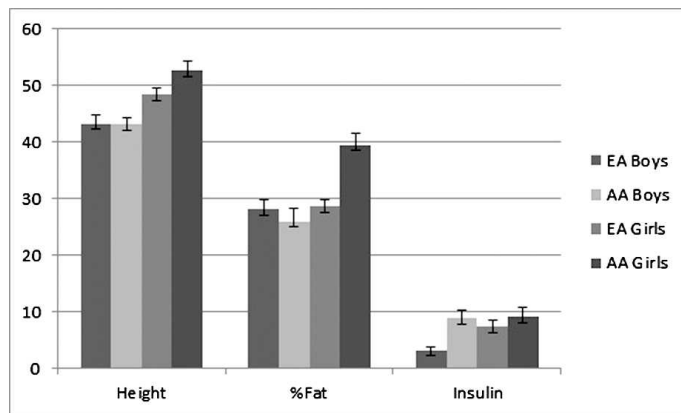
Fig 1. Height, percent fat and insulin concentration by race and sex

Table 3. Positive relationships between height and percent fat in children ages 4–10 years

	Total	
	R^2	P
Model A[a]		
4-10 y	.79	.04
Age 4	.34	.19
Age 5	.05	.93
Age 6	.36	.95
Age 7	.96	.02
Age 8	.36	.71
Age 9	.28	.34
Age 10	.39	.33
Model B[b]		
4-10 y	.77	.21
Age 7	.52	.08

[a] Model A evaluates the relationship between percent fat and height (adjusted for sex and race).
[b] Model B evaluates the relationship with insulin included in the models.

Table 4. Relationship between height and percent fat by race and sex

	Race			Sex	
	R^2	P		R^2	P
Model A[a]					
EA	.28	.41	Boys	.31	.72
AA	.77	.05	Girls	.93	.05
Model B[b]					
AA	.63	.08	Girls	.41	.20

[a] Model A evaluates the relationship between percent fat and height (adjusted for age, sex and race where appropriate).
[b] Model B evaluates the relationship with insulin included in the models.

opmental perturbations. Not only is developmental onset and progression accelerated earlier among AA females, our findings illustrate greatest adiposity levels in this group overall. Proximity to puberty indeed explains the findings of greater circulating insulin, a known metabolic characteristic specific to AA females.[12,19] Using longitudinal assessment, we have previously reported earlier age at menarche, as well as higher circulating post-pubertal reproductive hormones and lesser rebound in insulin sensitivity (post-puberty) in AA relative to EA girls.[19] Although the long-term effects have not yet been realized, given the confirmed role of adiposity and pubertal timing and tempo in the developmental origin of many chronic diseases,[12,14,18,20] the height-adiposity nexus may account for clinically significant, race- and sex-specific differences in health outcomes.

We observed a racial difference in BMC, which was at least partially attributed to height differences, particularly among obese AA, and may reflect accelerated growth patterning. A recent evaluation of height variation over the past few decades indicates that among EA men and women, average adult height began to increase around 1975 after nearly two decades of stagnation. However, an apparent sexual dimorphism among AA was observed, such that an increase in height was also observed in AA males (albeit to a lesser extent than observed in EA males), yet the height of AA females diminished.[21] As a key mitogenic signaling molecule, insulin likely influences growth velocity. Our findings support insulin as a mediator in growth-related processes involving linear growth and adipose tissue accrual, as the positive relationships found between height and percent fat was attenuated after accounting for fasting insulin concentration. African Americans are known to have generally greater circulating insulin concentrations compared to EA, and are at

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greater risk for hyperinsulinemia. Additionally, energy allocated among developing tissues is the product of contrasting pathways during growth to some degree.[22] In childhood, greater female adiposity, is evolutionarily related to trade-off investment in preparation for reproductive maturity.[22] As women in general have greater adiposity levels relative to men, accompanied by higher insulin concentration, it is possible that together synergistic effects are exerted, and are particularly apparent among AA females. The extent to which the relationship translates into health outcomes and whether these observed relationships contribute in part to decline in adult height and greater adverse health outcomes among AA women warrants further investigation.

Despite biologically-driven determination of height, the extent to which a person can reach maximal potential for physical stature is related to the intersection between biological and non-biological factors. Developmental and environmental processes that an individual interacts set a range of phenotypic outcomes. It is conceivable that a relationship between height, adiposity and future health outcomes may have increased expression of strategies shaped earlier in the life course by factors such as low birth weight, followed by compensatory rapid growth. In general, AA babies are about 250g smaller than EA babies, and tend to grow more rapidly postnatally. The accelerated postnatal growth pattern observed among AA may underlie disparities in cardiovascular disease and type 2 diabetes.[23] Communicating the importance of factors underlying developmental processes as an influence on health disparities will facilitate the understanding of how inherent and environmental factors interact to influence patterns of health and disease. There is growing appreciation that environmental factors contribute to health disparities by influencing biological processes, with varying impact throughout the lifecycle.

The use of robust body composition measures allowed for added accuracy in terms of fat mass quantification beyond the classically utilized BMI, which may confound race-related comparisons.[15] Although this study generates valuable insight regarding the contemporary height-fat relationship, limitations must be taken into consideration. Of note, the narrow age range of the boys in our study precludes speculation regarding peak height velocity and future health outcomes; however, among males, tallness at seven years has been associated with CVD risk with each 10cm increase in height increasing relative risk for CVD, primarily due to increased stroke risk.[23] This is consistent with the association between childhood linear growth and elevated blood pressure, the main risk factor for stroke. Future studies should include a larger sample size, inclusion of multiple races/ethnicities, as well as inclusion of individuals with a wider range of body habitus.

Taken together, pathways underlying height and adiposity seem to display positive directionality in young children undergoing rapid growth, with an apparent contribution by the circulating growth-related hormone insulin. Characteristic greater male leanness met with greater female adiposity, as well as earlier pubertal onset in females, was apparent in this sample. In the exaggerated state, as with adiposity, perturbation may be consequential in terms of adult stature through alteration of underlying metabolic pathways. The mitogenic effects of exaggerated levels of circulating insulin may augment growth-related processes, although the extent to which it manifests into health risk is not clear. It is known that while growth is highly organized, a rapid change in hormonal milieu (eg, leading to alterations in cell number and composition of muscle, adipose and bone)[24] may perturb the system ultimately disrupting tissue development ratios.[23] The degree of convergence throughout growth and development of height- and adiposity-related determinants of adulthood stature is unclear. Adiposity is known to increase chronic disease risk; however its impact is not equally manifested across populations. Paralleled sex and race differences in linear growth patterns may provide insight into adulthood cardiometabolic disease risk and warrants further study.

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Data analysis and interpretation: Hanks, Newton, Casazza
Manuscript draft: Hanks, Newton, Casazza
Statistical expertise: Casazza
Acquisition of funding: Casazza
Administrative: Casazza
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