ONLINE FIRST

Association of Pediatric Psoriasis Severity With Excess and Central Adiposity

An International Cross-Sectional Study

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Objective: To investigate the relationship of excess and central adiposity with pediatric psoriasis severity.

Design, Setting, and Participants: Multicenter, cross-sectional study of 409 psoriatic children. Psoriasis was classified as mild (worst Physician's Global Assessment score ≤3 with body surface area ≤10%) or severe (worst Physician's Global Assessment score ≥3 with body surface area >10%). Children were enrolled from 9 countries between June 19, 2009, and December 2, 2011.

Main Outcome Measures: Excess adiposity (body mass index percentile) and central adiposity (waist circumference percentile and waist to height ratio).

Results: Excess adiposity (body mass index ≥85th percentile) occurred in 37.9% of psoriatic children (n=155) vs 20.5% of controls (n=42) but did not differ significantly by severity. The odds ratio (95% CI) of obesity (body mass index ≥95th percentile) overall in psoriatic children vs controls was 4.29 (1.96-9.39) and was higher with severe (4.92; 2.20-10.99) than with mild (3.60; 1.56-8.30) psoriasis, particularly in the United States (7.60; 2.47-23.34, and 4.72; 1.43-15.56, respectively). Waist circumference above the 90th percentile occurred in 9.3% of the control (n=19), 14.0% of the mild psoriasis (n=27), and 21.2% of the of severe psoriasis (n=43) participants internationally; this incidence was highest in the United States (12.0% [n=13], 20.8% [16], and 31.1% [32], respectively). Waist to height ratio was significantly higher in psoriatic (0.48) vs control (0.46) children but was unaffected by psoriasis severity. Children with severe psoriasis at its worst, but mild at enrollment, showed no significant difference in excess or central adiposity from children whose psoriasis remained severe.

Conclusions: Globally, children with psoriasis have excess adiposity and increased central adiposity regardless of psoriasis severity. The increased metabolic risks associated with excess and central adiposity warrant early monitoring and lifestyle modification.

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PSORIASIS IS AN IMMUNE-mediated inflammatory skin disease that affects 2.5% to 3.2% of the global population.[1,2] Psoriasis begins during childhood in 22% to 33% of the cases, especially during adolescence,[2-5] and the incidence in children has more than doubled since the early 1970s.[3] Adults with psoriasis have an increased risk of obesity, myocardial infarction, stroke, and diabetes mellitus.[6-9] Recent studies also suggest the association of psoriasis with obesity in children. Of 211 North American children with moderate to severe psoriasis in an etanercept trial, 37% were obese (body mass index [BMI] ≥95th percentile).[10] Among 96 Italian children with mild to severe psoriasis, 48% were overweight (BMI ≥85th percentile) vs 27% of controls.[11] Using a German pediatric registry, obesity (by *International Classification of Diseases, 10th Revision* [*ICD-10*] code) occurred 1.7-fold more often in psoriatic children than controls.[5] In a US-based registry, overweight, moderately obese, and extremely obese children had 1.31-, 1.39-, and 1.78-fold greater odds, respectively, of having psoriasis (by *International Classification of Diseases, Ninth Revision* [*ICD-9*] code) than did children with normal weight.[12] These investigations provide evidence that children with psoriasis are at increased risk of being overweight or obese. However, ascertainment bias and underidentification are limitations of registry

studies, which rely on *ICD* codes for diagnosis of psoriasis and obesity rather than direct examination and measurements to calculate BMI. In addition, the risk of excess adiposity relative to psoriasis severity has received little attention. Increased waist circumference (WC) percentile[13-16] and waist to height ratio[15-20] are noninvasive surrogates for determination of central adiposity and more sensitive indicators for metabolic disease than is BMI percentile, including in children.[15,16,19,20] Waist circumference percentile is increased in adults with psoriasis[21] but has never been assessed in psoriatic children. Waist to height ratio has more recently been found to be a better predictor of cardiovascular risk than BMI or WC percentiles[17,19] but has never been assessed in adult or pediatric patients with psoriasis.

Using an international cohort of children with psoriasis, we examined the relationship between adiposity and psoriasis in children. Our goals were to (1) evaluate the effect of disease severity on the association of psoriasis with excess adiposity (being overweight or obese); (2) assess whether central obesity, as a surrogate for higher cardiovascular risk, was related to psoriasis severity; and (3) examine whether the association of excess adiposity with psoriasis varied regionally. We hypothesized that excess adiposity and central adiposity are most highly correlated with psoriasis of greater severity but that children with mild psoriasis are also at risk. Furthermore, we expected that psoriatic children in the United States would have a greater risk of excess and central adiposity compared with children from other countries.

METHODS

STUDY DESIGN AND POPULATION

A multicenter, international, cross-sectional study was performed to determine the relationship between adiposity and psoriasis severity in children. Participants were recruited between June 19, 2009, and December 2, 2011, from all children with psoriasis who were seen at 18 dermatology referral centers with psoriasis expertise in the Americas (Brazil, Canada, Chile, and the United States), Europe (Italy, the Netherlands, Turkey, and the United Kingdom), and Asia (Malaysia). Inclusion criteria included age 5 to 17 years and a 6-month or more history of plaque psoriasis. Diagnosis was confirmed by a psoriasis specialist. Siblings were excluded in both the psoriatic and control populations. Children of similar age and sex (but not matched for ethnicity) without skin or systemic inflammatory disease (eg, nevi, molluscum contagiosum, warts, and acne) and without a family history of psoriasis or psoriatic arthritis were recruited in the United States, the Netherlands, Italy, and Malaysia. To minimize ascertainment bias, an attempt was made to recruit all patients serially at presentation, and no potential participant refused. Parents and children, as required by each center's institutional review board or ethics committee, provided written informed consent. Investigators completed a questionnaire with each patient/parent that addressed patient history, race/ethnicity, severity of psoriasis at its worst, and history of psoriasis/psoriatic arthritis and metabolic disease in family members. A projected sample of 169 individuals per group provided 80% power to detect rates of excess adiposity from 22% among participants serving as controls to 37% among those with psoriasis.[10] Participants who indicated race as *other* (2 control, 3 with moderate psoriasis [MP], and 4 with severe psoriasis [SP]) were excluded from analysis of the impact of race because of their racial heterogeneity. Tanner stage was not examined, but a secondary analysis was performed on subsets of children aged 5 through 7 years and 15 through 17 years as representative of prepubertal and postpubertal participants on the basis of established puberty ranges.[22] Deidentified data were compiled centrally by the International Psoriasis Council, and statistical analysis was performed at Northwestern University, Chicago, Illinois.

ANTHROPOMETRIC MEASURES

Weight and height were measured and BMI was calculated as weight in kilograms divided by height in meters squared. An age- and sex-adjusted BMI percentile was assigned using the modified least mean square estimation procedure from the 2000 Centers for Disease Control and Prevention (CDC) growth charts.[23] Excess adiposity was defined as being either overweight or obese. Children with BMI values between the 85th percentile or higher and less than the 95th percentile were classified as overweight, and those with BMI values at the 95th percentile or above were classified as obese.[24,25] A BMI percentile of 5 or less was considered underweight, and a percentile between 5 and less than 85 was considered healthy weight. Waist circumference was measured midway between the most inferior rib and the superior border of the iliac crest with an inelastic measuring tape. The WC percentile was determined according to sex, age, and ethnicity-specific cutoffs[26] and was classified into 6 percentile groups, with the 2 highest being the 75th to 90th and greater than the 90th percentiles. Waist to height ratio was considered as a continuous measure of risk but, for estimating the odds of excess central adiposity defined by the waist to height ratio, cutoffs established by Kahn et al[19] were used to define high ($\geq$0.539) and intermediate ($\geq$0.490) levels of cardiovascular risk.

DETERMINATION OF PSORIASIS SEVERITY

Psoriasis severity was classified as mild or severe and was based primarily on Physician's Global Assessment (PGA)[27] score and secondarily on body surface area (BSA). The PGA was scored as 0 (none) to 5 (severe). To establish severity within the pediatric population, a PGA range of 4 to 5 was designated as SP, and a range of 1 to 2 was considered MP. The moderate PGA score of 3 was designated as MP if the BSA was 10% or less and as SP if the BSA was more than10%.[28] Peak severity historically was used to classify psoriasis as mild or severe, and severity was also determined at enrollment. For all participants, current treatment or a history of treatment with phototherapy and/or systemic medications was recorded. The same physician scored both the worst and current severity of psoriasis in the participants at each site to minimize the risk of per-patient or per-center interobserver variability.

STATISTICAL ANALYSIS

Descriptive statistics are presented as counts and percentages for categorical variables, means (SDs) for continuous data, and medians and interquartile ranges for psoriatic duration. Analyses include generalized linear mixed models for binary (logit link function), categorical (generalized logit link function), and ordinal (γ link function) outcome data and mixed models for outcomes that were normally distributed. All models included a random effect of study center and were adjusted for age, sex, continent, or race. Models comparing MP with SP were ad-

Table 1. Demographic and Metabolic Characteristics of All Participants by Psoriasis Severity

Characteristic	Comparison Group					
	Noninflammatory Control	Psoriasis	*P* Value[a]	MP at Peak	SP at Peak	*P* Value[b]
Participants, No. (%)	205 (33.4)	409 (66.6)		203 (33.1)	206 (33.6)	
Age, mean (SD), y	11.5 (3.8)	12.2 (3.6)	.97	11.8 (3.6)	12.5 (3.6)	.86
Male sex, No. (%)	96 (46.8)	178 (43.5)	.22	84 (41.4)	94 (45.9)	.77
Duration of psoriasis, median (IQR), y	. . .	4 (2-8)		4 (2-7)	5 (2-8)	.78
Race, No. (%)						
White, non-Hispanic	156 (76.1)	247 (60.5)		134 (66.0)	113 (55.1)	
Asian	18 (8.8)	84 (20.5)		33 (16.3)	51 (24.6)	
Hispanic or Latino	19 (9.3)	46 (11.2)	.48	20 (9.9)	26 (12.3)	.53
African American	8 (3.9)	13 (3.2)		5 (2.5)	8 (3.9)	
Other	4 (2.0)	19 (4.6)		11 (5.4)	8 (3.9)	
Continent, No. (%)						
Americas	108 (52.7)	200 (48.8)		89 (43.8)	111 (53.6)	
Europe	87 (42.4)	148 (36.1)	.98	90 (44.3)	58 (28.0)	.89
Asia	10 (4.9)	62 (15.1)		24 (11.8)	38 (18.4)	
Other characteristics, No. (%)						
Psoriatic arthritis	. . .	23 (5.6)		7 (3.5)	16 (7.7)	.72
Phototherapy[c]	. . .	88 (21.8)		18 (8.9)	70 (34.8)	**<.001**
Systemic medications[c]	. . .	104 (25.7)		22 (10.8)	82 (40.8)	**<.001**
Family history, No. (%)						
Diabetes mellitus	66 (41.8)	153 (48.1)	.25	66 (44.0)	87 (51.8)	.72
Hypertension	83 (52.5)	165 (52.2)	.95	77 (51.3)	88 (53.0)	.19
Hyperlipidemia	77 (48.7)	115 (36.2)	.66	53 (35.3)	62 (36.9)	.68
Obesity	48 (30.4)	94 (29.6)	.61	37 (24.7)	57 (33.9)	.71
Psoriatic arthritis	. . .	21 (6.6)	. . .	5 (3.3)	16 (9.5)	.76
Psoriasis, extended family	. . .	213 (52.0)	. . .	97 (47.8)	116 (56.0)	.17
Psoriasis, immediate family	. . .	118 (28.9)	. . .	56 (27.6)	62 (30.1)	.89
Metabolic characteristics, mean (SD)						
SBP, mm/Hg	114 (11)	110 (12)	**.008**	111 (12)	110 (12)	.55
DBP, mm/Hg	66 (9)	67 (8)	.80	68 (8)	66 (8)	**.049**
Height percentile	59.7 (30.9)	52.7 (32.2)	.51	52.6 (33.4)	52.9 (31.2)	.93
Weight percentile	59.7 (29.1)	62.6 (31.7)	**.03**	62.7 (31.0)	62.6 (32.4)	.80
BMI percentile	54.9 (29.6)	63.8 (31.8)	**<.001**	65.3 (30.0)	62.3 (33.4)	.29
BMI percentile, median (IQR)	56.4 (36.5-80.8)	71.6 (40.8-93.4)	**<.001**	73.3 (41.6-92.3)	69.6 (34.6-94.7)	.28
BMI category, No. (%)						
Underweight	13 (6.3)	25 (6.1)		10 (4.9)	15 (7.3)	
Healthy weight	150 (73.2)	229 (56.1)	**<.001**	115 (56.6)	114 (55.6)	.10
Overweight	27 (13.2)	72 (17.6)		44 (21.7)	28 (13.5)	
Obese	15 (7.3)	83 (20.2)		34 (16.8)	49 (23.7)	
Waist circumference, No. (%)						
<10th percentile	15 (7.4)	44 (11.1)		15 (7.8)	29 (14.3)	
10th to <25th	36 (17.7)	50 (12.6)		21 (10.9)	29 (14.3)	
25th to <50th	41 (20.1)	65 (16.4)		35 (18.1)	30 (14.8)	
50th to <75th	55 (27.0)	102 (26.0)	**.049**	59 (30.6)	43 (21.7)	.28
75th to 90th	38 (18.6)	64 (16.2)		36 (18.7)	28 (13.8)	
>90th	19 (9.3)	70 (17.7)		27 (14.0)	43 (21.2)	
Waist to height ratio, mean (SD)	0.46 (0.05)	0.48 (0.08)	**.002**	0.48 (0.07)	0.48 (0.09)	.38

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; ellipsis, not applicable; IQR, interquartile range; MP, mild psoriasis; SBP, systolic blood pressure; SP, severe psoriasis.

[a] Adjusted for fixed effects of age, sex, and continent and random effect of center. Boldface type indicates significant differences.

[b] Adjusted for fixed effects of age, sex, continent, phototherapy, systemic medications, and psoriasis duration and random effects of center. Boldface type indicates significant differences.

[c] Some patients had used both phototherapy and systemic immunosuppressant medications.

justed for systemic medication, phototherapy, and disease duration. Correlation between PGA and BSA severity scales was assessed using a Spearman rank correlation because the 2 measures are not on the same scale. Agreement between BMI categories and WC categories was assessed using a weighted κ. Interactions between psoriatic groups and age, race (or continent), and sex were assessed to gauge evidence of an effect modification; interaction terms were fit to examine the possibility of a differential effect of race on adiposity levels. When the interaction of race and psoriasis was significant, further analyses were stratified to determine the effect of race within psoriatic groups and vice versa. There was interest a priori in comparing psoriatic children vs controls and MP vs SP; hence, a significance level of .05 was used for all comparisons. This increases the chance of a type I error; however, many comparisons were done to assess whether the relationships observed in the primary analyses were seen in subgroups and were not intended to draw specific conclusions about subgroups. All analyses were run in commercial software (SAS, version 9.2; SAS Institute Inc).

Table 2. Demographic and Metabolic Characteristics of US Participants by Psoriasis Severity

Characteristic	Comparison Group					
	Noninflammatory Control	Psoriasis	*P* Value[a]	MP at Peak	SP at Peak	*P* Value[b]
No. (% of total)	108 (37.4)	181 (62.6)		78 (27.0)	103 (35.6)	
Age, mean (SD), y	11.3 (4.0)	12.6 (3.6)	.16	12.3 (3.6)	12.8 (3.6)	.59
Male sex, No. (%)	43 (39.8)	73 (40.3)	.83	27 (34.6)	46 (44.7)	.53
Duration of psoriasis, median (IQR), y	. . .	5 (2-9)	. . .	4 (2-8)	5 (2-9)	.99
Race, No. (%)						
White, non-Hispanic	73 (67.6)	110 (60.8)		49 (62.8)	61 (59.2)	
Asian	8 (7.4)	22 (12.2)		9 (11.5)	13 (12.6)	
Hispanic or Latino	17 (15.7)	33 (18.2)	.14	14 (18.0)	19 (18.5)	.96
African American	8 (7.4)	9 (5.0)		3 (3.9)	6 (5.8)	
Other	2 (1.9)	7 (3.9)		3 (3.9)	4 (3.9)	
Other characteristics, No. (%)						
Psoriatic arthritis	. . .	19 (10.5)	. . .	7 (9.0)	12 (11.7)	.59
Phototherapy[c]	. . .	40 (22.1)	. . .	6 (7.7)	34 (33.0)	**.001**
Systemic medications[c]	. . .	65 (35.9)	. . .	14 (17.9)	51 (49.5)	**.001**
Family history, No. (%)						
Diabetes mellitus	53 (49.1)	103 (56.9)	.16	44 (56.4)	59 (57.3)	.64
Hypertension	61 (56.5)	101 (55.8)	.32	48 (61.5)	53 (51.5)	.06
Hyperlipidemia	64 (59.3)	83 (45.9)	.96	37 (47.4)	46 (44.7)	.61
Obesity	41 (38.0)	62 (34.3)	.66	23 (29.5)	39 (37.9)	.66
Psoriatic arthritis	. . .	17 (9.4)		3 (3.9)	14 (13.6)	.16
Psoriasis, extended family	. . .	93 (51.4)		35 (44.9)	58 (56.3)	.28
Psoriasis, immediate family	. . .	55 (30.4)		20 (25.6)	35 (34.0)	.99
Metabolic characteristics, mean (SD)						
SBP, mm/Hg	110 (12)	110 (12)	.74	109 (11)	111 (12)	.52
DBP, mm/Hg	64 (10)	67 (8)	.46	67 (8)	67 (8)	.48
Height percentile	59.9 (28.6)	54.4 (31.9)	.56	52.3 (33.2)	56.1 (30.9)	.43
Weight percentile	59.8 (28.0)	68.0 (31.2)	**.04**	65.2 (31.9)	70.2 (30.7)	.66
BMI percentile	55.6 (28.8)	70.4 (30.1)	**<.001**	70.5 (28.9)	70.4 (31.1)	.54
BMI percentile, median (IQR)	56.4 (37.0-80.9)	82.7 (50.8-96.1)	**<.001**	83.0 (50.8-93.4)	80.8 (50.7-96.7)	.65
BMI category, No. (%)						
Underweight	4 (3.7)	7 (3.9)		4 (5.1)	3 (2.9)	
Healthy weight	83 (76.9)	88 (48.6)	**<.001**	37 (47.4)	51 (49.5)	.22
Overweight	12 (11.1)	36 (19.9)		22 (28.2)	14 (13.6)	
Obese	9 (8.3)	50 (27.6)		15 (19.2)	35 (34.0)	
Waist circumference, No. (%)						
<10th percentile	9 (8.3)	17 (9.4)		6 (7.8)	11 (10.7)	
10 to <25th	15 (13.9)	21 (11.7)		8 (10.4)	13 (12.6)	
25 to <50th	22 (20.4)	27 (15.0)	.13	11 (14.3)	16 (15.5)	.78
50 to <75th	31 (28.7)	42 (23.3)		24 (31.2)	18 (17.5)	
75 to 90th	18 (16.7)	25 (13.9)		12 (15.6)	13 (12.6)	
>90th	13 (12.0)	48 (26.7)		16 (20.8)	32 (31.1)	
Waist to height ratio, mean (SD)	0.46 (0.05)	0.49 (0.08)	**.01**	0.49 (0.06)	0.49 (0.10)	.97

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; ellipsis, not applicable; IQR, interquartile range; MP, mild psoriasis; SBP, systolic blood pressure; SP, severe psoriasis.

[a] Adjusted for fixed effects of age, sex, and race/ethnicity and random effect of center. Boldface type indicates significant differences.

[b] Adjusted for fixed effects of age, sex, race/ethnicity, phototherapy, systemic medications, and psoriasis duration and random effect of center. Boldface type indicates significant differences.

[c] Some patients had used both phototherapy and systemic immunosuppressant medications.

RESULTS

PSORIASIS SEVERITY AND EXCESS ADIPOSITY IN CHILDREN

Of 614 children enrolled from 9 countries, 203 (33.1%) had MP and 206 (33.6%) had SP based on assessment of peak severity; 205 (33.4%) age- and sex-comparable children without inflammatory disorders served as controls (**Table 1**). Age and sex distribution were similar among regions, although ethnicity varied, reflecting different populations regionally. The classification based on PGA severity correlated well with severity based on BSA (r_s=0.76, P=.001). Severity classification was further validated by the use of phototherapy and/or systemic immunosuppressant medications in 56.5% of children internationally and 65.3% of US participants with SP (vs 1.68% and 21.8% with MP, respectively). Having a history of diabetes mellitus, hypertension, hyperlipidemia, obesity, psoriasis, or psoriatic arthritis in immediate family members was not significantly different in the SP vs MP groups (Table 1 and **Table 2**). Categories of adiposity defined by BMI and WC percentiles moderately agreed (weighted κ_w=0.55; 95% CI, 0.50-0.61). The mean age of children with psoriasis was 12.2 years, with no significant difference between the MP and SP groups

Table 3. Age-, Sex-, Race/Continent–, and Center-Adjusted ORs

Predicting	Referent Control	Comparison	OR (95% CI)[a] BMI Percentile Threshold[b]	WC Percentile Threshold[c]	Waist to Height Ratio Threshold[d]
All participants internationally					
Overweight + obesity (excess adiposity)	Healthy weight	Psoriasis vs control	**2.65 (1.70-4.15)**	1.42 (0.96-2.10)	1.45 (0.96-2.19)
		MP vs control	**2.76 (1.69-4.50)**	1.30 (0.83-2.04)	1.35 (0.85-2.15)
		SP vs control	**2.56 (1.57-4.17)**	1.54 (0.99-2.41)	1.56 (0.98-2.48)
Obesity	Healthy weight	Psoriasis vs control	**4.29 (1.96-9.39)**	**2.52 (1.24-5.12)**	**3.10 (1.39-6.90)**
		MP vs control	**3.60 (1.56-8.30)**	1.90 (0.90-4.01)	2.21 (0.92-5.32)
		SP vs control	**4.92 (2.20-10.99)**	**3.06 (1.53-6.15)**	**4.10 (1.80-9.31)**
Obesity	Overweight	Psoriasis vs control	1.93 (0.89-4.15)	1.77 (0.85-3.67)	**2.88 (1.19-6.99)**
		MP vs control	1.38 (0.63-3.05)	1.37 (0.62-3.06)	1.67 (0.64-4.38)
		SP vs control	**2.85 (1.26-6.42)**	**2.36 (1.04-5.39)**	**5.11 (1.96-13.34)**
US participants					
Overweight + obesity (excess adiposity)	Healthy weight	Psoriasis vs control	**4.02 (2.11-7.63)**	**1.77 (1.03-3.07)**	**1.77 (1.02-3.09)**
		MP vs control	**4.22 (2.05-8.67)**	1.44 (0.75-2.78)	1.45 (0.75-2.79)
		SP vs control	**3.87 (1.95-7.70)**	**2.05 (1.12-3.76)**	**2.06 (1.12-3.81)**
Obesity	Healthy weight	Psoriasis vs control	**6.61 (2.16-20.17)**	**3.47 (1.39-8.66)**	**4.87 (1.51-15.76)**
		MP vs control	**4.72 (1.43-15.56)**	2.05 (0.80-5.25)	2.49 (0.71-8.74)
		SP vs control	**7.60 (2.47-23.34)**	**3.85 (1.64-9.00)**	**6.62 (2.11-20.76)**
Obesity	Overweight	Psoriasis vs control	1.61 (0.51-5.06)	**3.29 (1.22-8.87)**	**4.28 (1.33-13.75)**
		MP vs control	0.93 (0.31-2.84)	2.51 (0.84-7.48)	1.41 (0.48-4.12)
		SP vs control	2.96 (0.99-8.86)	**4.24 (1.33-13.46)**	**7.53 (2.29-24.78)**

Abbreviations: BMI, body mass index; MP, mild psoriasis; OR, odds ratio; SP, severe psoriasis; WC, waist circumference.

[a] Boldface type indicates significant differences.

[b] Overweight and obesity were defined as the 85th percentile or greater or the 95th percentile or greater, respectively, of BMI for age and sex; healthy weight was defined as between the 5th and 85th percentiles.

[c] Overweight and obesity were defined as greater than the 75th or greater than the 90th percentile, respectively, of WC for age, sex, and race; healthy weight was defined as between the 10th and 75th percentiles.

[d] Overweight and obesity were defined as a waist to height ratio of 0.490 or greater or 0.539 or greater, respectively. Participants with a waist to height ratio less than 0.377 (the lower 5% of our cohort) were eliminated from analysis, since they may be considered underweight, although the conclusions remained consistent when these participants were included as normal/healthy waist to height ratio.

(Table 1). A significantly higher percentage of children with psoriasis than controls showed excess adiposity (37.9% vs 20.5%) or obesity (20.2% vs 7.3%) ($P<.001$). The odds ratio (OR) for excess adiposity in psoriatic children of all severities vs controls was 2.65 (95% CI 1.70-4.15) and for obesity was 4.29 (1.96-9.39); similarly, in the United States the OR for excess adiposity was 4.02 (2.11-7.63) and for obesity was 6.61 (2.16-20.17) (**Table 3**). There was no modification by age ($P=.91$), pubertal status ($P=.58$), or age group ($P=.97$). Disease duration did not correlate with excess adiposity (Spearman correlation coefficient, 0.008).

OBESITY VS OVERWEIGHT IN SEVERE PSORIASIS INTERNATIONALLY

More children with SP than with MP were obese (controls, 7.3%; MP group, 16.8%; and SP group, 23.7%; $P<.001$) (Table 1); the OR for obesity (vs healthy weight) was 4.92 (95% CI, 2.20-10.99) for SP and 3.60 (1.56-8.30) for the MP group (Table 3). In the United States, obesity was seen in 8.3% of controls and 19.2% of children with MP but occurred in 34.0% of children with SP ($P=.01$); the OR for being obese (vs healthy weight) was 4.72 (95% CI, 1.43-15.56) for the MP group but 7.60 (2.47-23.34) for the SP group (Tables 2 and 3). Among children with excess adiposity, those with SP had the highest odds of obesity (OR, 2.85; 95% CI, 1.26-6.42) internationally, whereas the odds of obesity were not increased for the MP group compared with controls (Table 3).

PSORIASIS SEVERITY AND CENTRAL ADIPOSITY

Internationally, the odds of a WC percentile higher than 90 were significantly greater for children with psoriasis overall vs controls (OR, 2.52; 95% CI, 1.24-5.12) and the SP group vs controls (3.06; 1.53-6.15) but not the MP group vs controls (1.90; 0.90-4.01) (Tables 1 and 3). In the United States, the OR of having a WC percentile higher than the 75th or 90th was significantly increased in psoriasis overall vs controls (1.77; 95% CI, 1.03-3.07, and 3.47; 1.39-8.66, respectively) and the SP group vs controls (2.05; 1.12-3.76, and 3.85; CI 1.64-9.00, respectively) but not the MP group vs controls (Tables 2 and 3). Waist to height ratios were significantly higher in children with psoriasis overall than in controls internationally ($P=.002$) and in the United States ($P=.01$) (Tables 1 and 2). In parallel with WC percentiles, the OR of a waist to height ratio of 0.539 or greater was significantly higher for children with psoriasis overall vs controls (3.10; 95% CI, 1.39-6.90) and the SP group vs controls (4.10; 1.80-9.31) but not the MP group vs controls (2.21; 0.92-5.32) (Table 3). In the United States, the OR of having

Table 4. Comparison of Demographic and Metabolic Features by Continent (International) and Race (United States)[a]

Characteristic	Comparison Group: Noninflammatory Control			Comparison Group: Psoriasis			*P* Values[b]	
	Americas (n = 108)	Europe (n = 87)	Asia (n = 10)	Americas (n = 200)	Europe (n = 148)	Asia (n = 62)	Interaction	Race/ Continent
Age, mean (SD), y	11.3 (4.0)	11.5 (3.6)	13.0 (4.1)	12.6 (3.6)	11.5 (3.5)	12.4 (3.7)	.41	.15
Male sex, No. (%)	43 (39.8)	46 (52.9)	7 (70.0)	84 (42.0)	63 (42.6)	32 (51.6)	.72	.62
Duration of psoriasis, median (IQR), y	. . .	. . .		5 (2-9)	3 (1-6)	5 (2-9)	. . .	.82
Weight percentile, mean (SD)	59.8 (28.0)	62.6 (27.8)	32.1 (39.5)	67.5 (30.6)	65.7 (25.9)	39.7 (37.5)	.75	**<.001**
BMI percentile, mean (SD)	55.6 (28.8)	56.0 (29.3)	37.3 (37.9)	69.9 (29.9)	62.8 (29.1)	46.6 (37.1)	.69	**.001**
BMI category (%)								
Underweight	4 (3.7)	6 (6.9)	3 (30.0)	7 (3.5)	6 (4.1)	12 (19.4)	.21	.09
Healthy weight	83 (76.8)	62 (71.3)	5 (50.0)	101 (50.5)	97 (65.5)	32 (51.6)		
Overweight	12 (11.1)	15 (17.2)	0 (0)	40 (20.0)	22 (14.9)	10 (16.1)		
Obese	9 (8.3)	4 (4.6)	2 (20.0)	52 (26.0)	23 (15.5)	8 (12.9)		
Waist circumference, No. (%)								
<10th	9 (8.3)	3 (3.5)	3 (30.0)	18 (9.1)	13 (9.6)	13 (21.3)	.89	**.002**
10th to <25th	15 (13.9)	19 (22.1)	2 (20.0)	22 (11.1)	17 (12.5)	11 (18.0)		
25th to <50th	22 (20.4)	17 (19.8)	2 (20.0)	29 (14.6)	24 (17.7)	12 (19.7)		
50th to <75th	31 (28.7)	23 (26.7)	1 (10.0)	51 (25.6)	46 (33.8)	6 (9.8)		
75th to 90th	18 (16.7)	20 (23.3)	0 (0)	29 (14.6)	24 (17.7)	11 (18.0)		
>90th	13 (12.0)	4 (4.7)	2 (20.0)	50 (25.1)	12 (8.8)	8 (13.1)		
Waist to height ratio	0.46 (0.05)	0.45 (0.05)	0.46 (0.07)	0.49 (0.08)	0.46 (0.07)	0.47 (0.07)	.66	**.02**

Characteristic	Hispanic/ African American			Hispanic/ African American			*P* Value	
	White (n = 73)	(n = 25)	Asian (n = 8)	White (n = 110)	(n = 42)	Asian (n = 22)	Interaction	Race/ Continent
Age, mean (SD), y	11.6 (4.1)	10.2 (4.1)	11.9 (3.0)	12.6 (3.5)	12.6 (3.7)	13.0 (4.0)	.43	.52
Male sex, No. (%)	29 (39.7)	10 (40.0)	4 (50.0)	48 (43.6)	12 (28.6)	11 (50.0)	.51	.27
Duration of psoriasis, median (IQR), y	. . .	. . .		2 (2-10)	4 (2-8)	6 (4-8)	. . .	.10
Weight percentile, mean (SD)	59.6 (27.2)	62.0 (28.2)	54.6 (38.2)	68.0 (29.3)	77.3 (27.0)	52.4 (40.7)	.49	**.006**
BMI percentile, mean (SD)	53.4 (28.1)	63.0 (26.8)	54.1 (40.4)	68.9 (29.2)	81.8 (22.4)	57.9 (38.0)	.57	**.002**
BMI category								
Underweight	2 (2.7)	1 (4.0)	1 (12.5)	2 (1.8)	1 (2.4)	3 (13.6)	.61	**.02**
Healthy weight	59 (80.8)	18 (72.0)	4 (50.0)	59 (53.6)	16 (38.1)	10 (45.5)		
Overweight	7 (9.6)	3 (12.0)	2 (25.0)	25 (22.7)	9 (21.4)	1 (4.6)		
Obese	5 (6.9)	3 (12.0)	1 (12.5)	24 (21.8)	16 (38.1)	8 (36.4)		
Waist circumference, No. (%)								
<10th	8 (11.0)	1 (4.0)	0 (0.0)	8 (7.3)	1 (2.4)	7 (31.8)	.76	**.001**
10th to <25th	10 (13.7)	2 (8.0)	2 (25.0)	17 (15.6)	2 (4.8)	2 (9.1)		
25th to <50th	10 (13.7)	10 (40.0)	2 (25.0)	13 (11.9)	12 (28.6)	1 (4.6)		
50th to <75th	22 (30.1)	7 (28.0)	1 (12.5)	32 (29.4)	5 (11.9)	3 (13.6)		
75th to 90th	14 (19.2)	3 (12.0)	1 (12.5)	15 (13.8)	10 (23.8)	0 (0.0)		
>90th	9 (12.3)	2 (8.0)	2 (25.0)	24 (22.0)	12 (28.6)	9 (40.9)		
Waist to height ratio	0.46 (0.05)	0.47 (0.06)	0.47 (0.06)	0.47 (0.08)	0.51 (0.08)	0.50 (0.10)	.82	**.02**

Abbreviations: BMI, body mass index; ellipsis, not applicable; IQR, interquartile range.

[a] Hispanic and black/African American children were combined because of their lower sample size and similar metabolic characteristics. Because of the small sample sizes and heterogeneity of the group, individuals who indicated race as *other* were excluded from this analysis.

[b] Boldface type indicates significant differences.

at least a waist to height ratio above the normal range (≥0.490) was also increased in psoriasis overall (1.77; 95% CI, 1.02-3.09) and in the SP group (2.06; 1.12-3.81) but not in the MP group (1.45; 0.75-2.79) (Table 3). Disease duration did not affect central adiposity (Spearman correlation coefficients,–0.008 and –0.010 for WC category and waist to height ratio, respectively).

ASSOCIATION OF EXCESS ADIPOSITY AND CENTRAL ADIPOSITY WITH PSORIASIS IN US CHILDREN

The difference in excess adiposity rates between psoriatic patients and controls was greatest in the Americas vs other continents ($P < .001$) (**Table 4** and **Figure 1**)

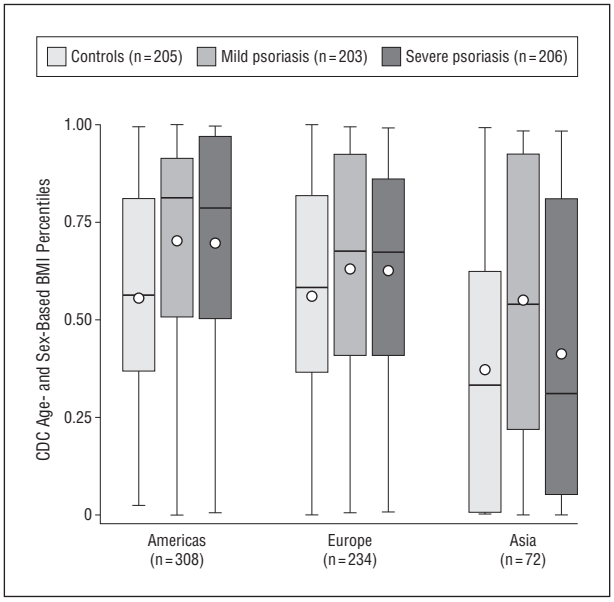

Figure 1. Box and whisker plots of body mass index (BMI) percentiles, defined using Centers for Disease Control and Prevention (CDC) growth charts, by psoriasis disease severity and continent of study participants. Open circles within the box plots represent group means and horizontal lines indicate medians. Boxes represent the interquartile range and whiskers indicate the range.

and in US vs non-US sites (P = .002) (**Table 5**). In addition, differences in central adiposity were greater in the Americas vs other continents (WC percentile, P = .002; waist to height ratio, P = .02) (Table 4) and in US vs non-US psoriatic patients (WC percentile, P = .015; waist to height ratio, P = .048) (Table 5). The excess adiposity in psoriatic patients vs controls was similar across US racial groups (Table 4). However, significantly greater rates for excess adiposity were seen in US Hispanics and African Americans (59.5%) compared with whites (44.5%) and Asians (40.0%) (P = .03), and both WC percentiles and waist to height ratios were higher in African Americans, Hispanics, and Asians than in whites (P = .001 and P = .02, respectively) (Table 4).

CLINICAL IMPROVEMENT AND THE ODDS OF OBESITY

No significant difference was noted for children with SP whose psoriasis transitioned to MP vs children with SP whose condition remained SP in the odds of having excess adiposity (OR, 1.34; 95% CI, 0.70-2.59), obesity (0.67; 0.31-1.43), or central adiposity (0.88; 0.45-1.72). Internationally, 136 children (66.0%) with SP had transitioned to MP by enrollment, 59.6% of whom used phototherapy and/or systemic medications (19.2% phototherapy, 20.0% systemic immunosuppressants, and 20.0% both). Sex (P = .70), age (P = .28), duration (P = .28), systemic medication use (P = .48), or continent (P = .34) did not predict transition. By enrollment, 67 US children (65.1%) with SP had transitioned to MP. Sex (P = .54), age (P = .08), duration (P = .13), systemic medication use (P = .29), or phototherapy (P = .12) similarly did not correlate with transition, although whites were more likely to improve than nonwhites (78.7% vs 45.2%; P = .001) and transition was more likely among younger patients (OR, 0.82; 95% CI, 0.07-0.97; P = .02).

COMMENT

The prevalence of childhood obesity has increased dramatically worldwide,[29-32] although a recent study shows stabilization.[33] Being overweight or obese during childhood is associated with an increased risk of sleep apnea,[34] cardiovascular risk factors,[35] insulin resistance, orthopedic complications,[36,37] and mortality resulting from cardiovascular disease in adulthood.[38] Our large cross-sectional study overcomes the limitations of registry data and further supports the association of pediatric psoriasis with increased BMI percentile. Children with psoriasis internationally, regardless of severity, have significantly greater odds than controls of being overweight or obese and thus are at increased risk of complications related to excess adiposity. Most children with MP who had excess adiposity were overweight but not obese, while most children with SP who had excess adiposity were obese. Consistently, the odds of obesity were increased in children with MP (OR, 3.60) but were much higher for children with SP (OR, 4.92), particularly in the United States (OR, 6.61). These ORs are considerably greater than those for adults in the United Kingdom with SP (OR, 1.79) and MP (OR, 1.27)[8] and for metabolic syndrome in US adults with psoriasis of all severities (OR, 1.96),[39] suggesting a greater association of obesity and psoriasis with childhood-onset vs adult-onset psoriasis. The particularly high odds of obesity in US children with psoriasis suggest that environment habits (higher caloric diet and less exercise) may affect the risk.

The BMI percentile remains the standard method for identifying overweight and obese pediatric patients,[40] but WC and particularly waist to height ratio are surrogates for central/visceral adiposity that are considered better indicators than BMI of metabolic risk.[13,14,17,18,41] Pediatric studies[15,16,19,42-46] have found WC above the 90th percentile and, even more so, high waist to height ratio to correlate better than BMI percentile with a higher risk of hypertension, hypertriglyceridemia, low high-density lipoprotein cholesterol level, and fasting insulin level. Our data demonstrate that children with SP (but not MP) have higher odds than controls of having a high WC percentile and waist to height ratio and thus have additional risks associated with central adiposity.

With a nonblinded cross-sectional design, ascertainment and selection biases are inherent risks of a study. However, given that all children with psoriasis were solicited and agreed to participate, ascertainment bias was limited in the MP and SP groups; because measures of disease severity (PGA score and BSA) were assessed per standard procedure and by the same physician, disease severity was also measured without bias. Although selection bias for controls without inflammation is possible, all eligible children without inflammatory disease were asked to participate; as seen in **Figure 2**, the distribution of percentiles was approximately uniform, as would be expected in a completely random sample. To establish growth standards for children older than 5 years,

Table 5. United States vs Non–United States Comparison of Demographic and Metabolic Characteristics

Characteristic	Comparison Group: Noninflammatory Control			Comparison Group: Psoriasis			Group by US Interaction, *P* Value[a]
	United States	Non–United States	*P* Value[a]	United States	Non–United States	*P* Value[b]	
No.	108	97		181	228		
Age, mean (SD), y	11.3 (4.0)	11.6 (3.6)	.51	12.6 (3.6)	11.9 (3.6)	.30	.30
Male sex, No. (%)	43 (39.8)	53 (54.6)	.50	73 (40.3)	105 (46.1)	.48	.74
Duration of psoriasis, median (IQR), y	. . .	. . .	. . .	5 (2-9)	4 (2-7)	. . .	. . .
Race, No. (%)							
White, non-Hispanic	73 (67.6)	83 (85.6)		110 (60.8)	137 (60.1)		**.04**
Asian	8 (7.4)	10 (10.3)		22 (12.2)	62 (27.2)		
Hispanic or Latino	17 (15.7)	2 (2.1)	**.004**	33 (18.2)	13 (5.7)	.60	
African American	8 (7.4)	0 (0)		9 (5.0)	4 (1.8)		
Other	2 (1.9)	2 (2.1)		7 (3.9)	12 (5.3)		
Other characteristics, No. (%)							
Psoriatic arthritis	. . .	. . .	. . .	19 (10.5)	4 (1.8)	**.03**	. . .
Phototherapy	. . .	. . .	. . .	40 (22.7)	48 (21.2)	.41	. . .
Systemic medications	. . .	. . .	. . .	65 (36.9)	39 (17.2)	.18	. . .
Family history, No. (%)							
Diabetes mellitus	53 (49.1)	13 (26.0)	.19	103 (56.9)	50 (36.8)	.08	.60
Hypertension	61 (56.5)	22 (44.0)	.87	101 (55.8)	64 (47.1)	.37	.18
Hyperlipidemia	64 (59.3)	13 (26.0)	.15	83 (45.9)	32 (23.5)	.055	.54
Obesity	41 (38.0)	7 (14.0)	.60	62 (34.3)	32 (23.5)	.57	.90
Psoriatic arthritis	. . .	. . .	. . .	17 (9.4)	4 (2.9)	.76	
Psoriasis, extended family	. . .	. . .	. . .	93 (51.4)	120 (52.6)	.51	
Psoriasis, immediate family	. . .	. . .	. . .	55 (30.4)	63 (27.6)	.42	
Metabolic characteristics, mean (SD)							
SBP, mm/Hg	110 (12)	118 (10)	.08	110 (12)	111 (12)	.83	.16
DBP, mm/Hg	64 (10)	69 (7)	.09	67 (8)	67 (9)	.93	.25
Height percentile	59.9 (28.6)	59.6 (33.4)	.86	54.4 (31.9)	51.3 (32.5)	.56	.85
Weight percentile	59.8 (28.0)	59.5 (30.4)	.92	68.0 (31.2)	58.4 (31.5)	.13	.39
BMI percentile	55.6 (28.8)	54.1 (30.6)	.82	70.4 (30.1)	58.6 (32.2)	.06	.30
BMI percentile, median (IQR)	56.4 (37.0-80.9)	56.4 (29.3-78.9)	.10	82.7 (50.8-96.1)	64.7 (33.7-89.1)	**.04**	.44
BMI category, No. (%)							
Underweight	4 (3.7)	9 (9.2)		7 (3.9)	18 (7.9)		
Healthy weight	83 (76.9)	67 (69.1)	.73	88 (48.6)	141 (61.8)	**.02**	.24
Overweight	12 (11.1)	15 (15.5)		36 (19.9)	36 (15.8)		
Obese	9 (8.3)	6 (6.2)		50 (27.6)	33 (14.5)		
Waist circumference, No. (%)							
<10th percentile	9 (8.3)	6 (6.3)		17 (9.4)	27 (12.6)		
10th to <25th	15 (13.9)	21 (21.9)		21 (11.7)	29 (13.5)		
25th to <50th	22 (20.4)	19 (19.8)	.48	27 (15.0)	38 (17.7)	**.02**	.56
50th to <75th	31 (28.7)	24 (25.0)		42 (23.3)	60 (27.9)		
75th to 90th	18 (16.7)	20 (20.8)		25 (13.9)	39 (18.4)		
>90th	13 (12.0)	6 (6.3)		48 (26.7)	22 (10.2)		
Waist to height ratio	0.46 (0.05)	0.45 (0.05)	.62	0.49 (0.08)	0.47 (0.07)	**.048**	.21

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; ellipsis, not applicable; IQR, interquartile range; SBP, systolic blood pressure.
[a] Adjusted for fixed effects of age, sex, and random effect of center. Boldface type indicates significant differences.
[b] Adjusted for age, sex, race, systemic medication, phototherapy, and psoriasis duration. Boldface type indicates significant differences.

both the CDC and the World Health Organization used the 1977 National Center for Health Statistics data. The CDC standards were selected for this study because they were the more conservative measure and were more likely to identify children who were overweight and obese.[47] International growth standards, including distribution for WC and waist to height ratio, should be developed.

The BMI percentile distributions showed increased adiposity in both American and European participants with MP and SP but only in children with MP from Asia. The reason for the lower mean BMI percentile of Asian children with SP is under investigation; a recent study demonstrated higher proportions of both obese and underweight children in the Chinese population.[48] It is possible that the differences in diet and exercise between the American/European countries and Malaysia, as well as genetic variations, could also account for regional variations in adiposity. Nevertheless, the small sample size, relatively small Asian control group, and large percentage of underweight Asian children with SP (24%) limit our data interpretation. The ethnicity-adjusted cutoffs for WC percentile were based on more than 9000 US children of African, Mexican, or European descent but not Asian descent,[26] which could explain the difference in WC

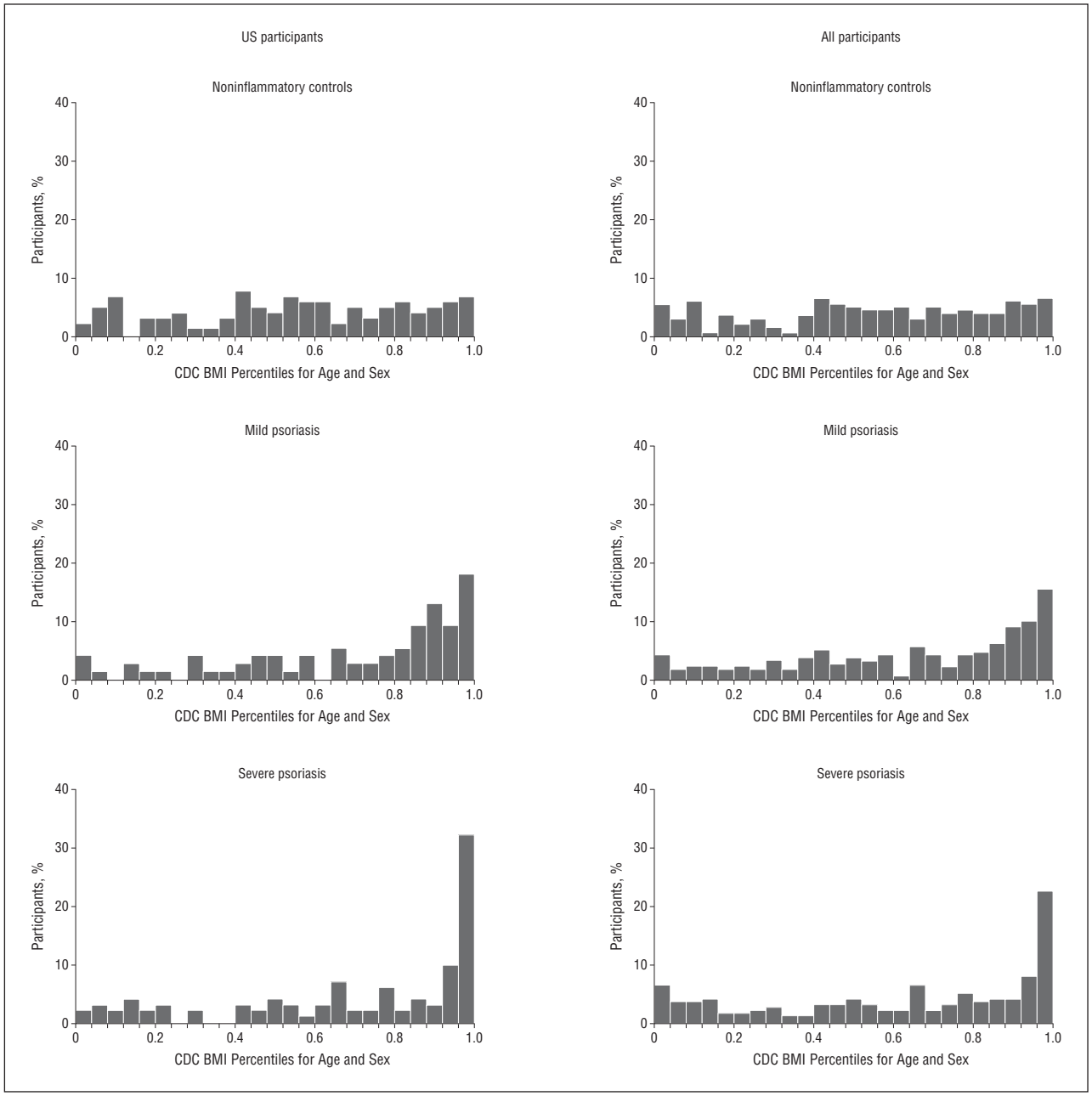

Figure 2. Histograms of body mass index (BMI) percentiles based on age- and sex-specific Centers for Disease Control and Prevention (CDC) growth charts by study groups in the US and international cohorts.

percentile distribution in control Asian children vs other ethnic groups. Indeed, central adiposity varies by ethnic origin among the Malay population,[49] and our questionnaire did not distinguish among ethnic subtypes or socioeconomic status, both of which can affect the genetic and environmental factors that influence adiposity.

The underlying basis for the relationship between excess adiposity and psoriasis is not well understood. However, overproduction of types 1 and 17 helper T-cell inflammatory cytokines is associated with both obesity[50] and psoriasis[51] in adults, suggesting that chronic inflammation drives both disorders. Indeed, remission of severe psoriasis has been described in adults after substantial weight loss as a result of gastric bypass surgery.[52,53] Treatment of psoriatic adults with cyclosporine and a 24-week weight loss diet (which reduced BMI and waist size) led to a greater reduction in psoriasis severity than did cyclosporine alone,[54] further suggesting a relationship between psoriasis and obesity.

Despite the clear association of psoriasis with obesity, an unanswered question is whether high BMI is the precursor of psoriasis in children or whether psoriasis leads to an increased BMI percentile through chronic cytokine release from psoriatic tissue, compounded by a lifestyle that may favor excess adiposity (eg, less physical activity and increased risk of depression).[55,56] A recent prospective cohort study[21] of 892 affected women found that increased adiposity preceded the occurrence of new-onset psoriasis; we are currently addressing whether increased adiposity precedes psoriasis onset in children.

In our study, children with SP whose psoriasis had transitioned to MP at enrollment showed no significant difference in adiposity from children with SP whose condition remained severe, despite controlling for other factors. Although not longitudinal, these data suggest that effective intervention for psoriasis may not alter the tendency toward adiposity. A possible confounder for this conclusion is the reported association of the use of tumor necrosis factor (TNF) inhibitors and increases in BMI in adults with psoriasis, hypothesized to result primarily from suppression of TNF-induced myocyte catabolism.[16,20,57,58] Although the numbers of children with SP administered TNF inhibitors (etanercept, adalimumab, and/or infliximab) by enrollment (23 of 82 using systemic medications globally and 17 of 51 in the United States) were insufficient for statistical comparison, 52% of children with SP globally (59% in the United States) administered TNF inhibitors remained overweight or obese vs 41% of children with SP globally (52% in the United States) administered other systemic immunosuppressants. The possibility that use of TNF inhibitors in children leads to weight gain, despite the ameliorative effects on inflammation, deserves further investigation.

In conclusion, children with psoriasis internationally, regardless of severity, are more likely to be overweight or obese and thus are at increased risk for complications related to excess adiposity. The association of central adiposity is greatest in children with severe psoriasis, and monitoring of these patients should be especially vigilant. Should further studies show excess adiposity to be a precursor for psoriasis, attempts at early weight loss and lifestyle modification will be important, not only to decrease the risk of metabolic disease but also to modulate the course of pediatric psoriasis.

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