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Visceral fat is associated with the racial differences in liver fat between black and white adolescent boys with obesity

SoJung Lee, Ph.D.[1] and **Jennifer L. Kuk, Ph.D.**[2]

[1]Division of Weight Management & Wellness, Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh School of Medicine, Pittsburgh, PA 15224

[2]School of Kinesiology and Health Science, York University, Toronto, Ontario, Canada M3J1P3

Abstract

Objective—We examined whether racial differences in liver fat is associated with the differences in abdominal fat distribution or cardiorespiratory fitness (CRF).

Methods—Participants included 57 black and white obese boys (12–18 yrs). Total and abdominal fat was measured by DEXA and MRI, respectively. CRF was measured using a maximal graded treadmill test with the use of standard open-circuit spirometry techniques until volitional fatigue. Liver fat was measured using a 3T proton magnetic resonance spectroscopy. Fatty liver was defined as having liver fat ≥5%.

Results—In the sample, 16.1% of black boys and 30.8% of white boys had fatty liver. Liver fat was associated ($P \leq 0.05$) with BMI percentile ($r=0.28$), total fat ($r=0.31$), waist circumference ($r=0.38$), visceral fat ($r=0.62$), ASAT ($r=0.30$), and CRF ($r= -0.27$) adjusting for age and race. White boys had greater liver fat than black boys with adjustment for age and differences in BMI percentile or CRF, but not with waist circumference or visceral fat ($P>0.05$). In a model with age, ethnicity, total body fat, fat free mass, visceral fat, abdominal subcutaneous fat and CRF, visceral fat was the only factor to be independently associated with increased odds of having fatty liver (OR= 1.12, 95% CI: 1.04–1.21, $P=0.003$).

Conclusion—The racial disparities in liver fat between obese black versus white adolescents are explained, in part, by differences in visceral fat.

Keywords

Liver fat; non-alcoholic fatty liver disease; visceral adipose tissue; race

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of conditions defined by abnormal triglyceride accumulation in liver (1). Currently, NAFLD is the most common

All correspondence and reprint requests addressed to: SoJung Lee, Ph.D., Division of Weight Management & Wellness, Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh School of Medicine, 4401 Penn Ave, Faculty Pavilion (Office 6104), Pittsburgh, PA 15224, Phone: (412) 692-5147, Fax: (412) 692-8531, SoJung.Lee@chp.edu.

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form of liver disease and is strongly linked with obesity, metabolic inflexibility (2), insulin resistance and type 2 diabetes in youth (3, 4).

The prevalence of NAFLD significantly differs by race and ethnicity, such that white children and adolescents have 2.7 times greater risk of NAFLD than their black peers based on studies using liver histology (5). Similarly, using a non-invasive magnetic resonance imaging (MRI) obese white adolescents are reported to have substantially higher liver fat content (17.5%) compared with undetectable liver fat in obese black adolescents despite having similar total body fat (6). Given that black obese adolescents have greater diabetogenic risk profiles (e.g., lower insulin sensitivity and hyperinsulinemia) than their white peers (7, 8), it is unclear why black adolescents are less prone to NAFLD than their white peers.

Although the pathogenesis of pediatric NAFLD remains unclear, visceral adiposity is suggested to be an important culprit for increased liver fat in youth (9, 10). We (11, 12) and others (6, 13) demonstrated that black youth have significantly lower levels of visceral fat than their white peers despite similar degree of total adiposity. Although it has been speculated that the lower visceral adiposity in black youth may play a protective role against fatty liver compared with their white peers (6), no studies have directly examined the potential contributing factors that may explain the racial disparities in NAFLD in youth. Therefore, we examined whether racial differences in liver fat in obese black versus white adolescents are attributed to differences in total and regional body fat distribution, including visceral fat, or cardiorespiratory fitness (CRF).

METHODS

The study sample included 31 black and 26 white obese boys (BMI $\geq 95^{th}$, 12–18 yrs) who underwent ^{1}H-MRS test to quantify liver fat. Participants were recruited via public advertisements and from the Weight Management and Wellness Center at Children's Hospital of Pittsburgh. All subjects were non-smokers, non-diabetic, physically inactive and not taking medications known to affect study outcomes. None of the participants had liver disease or consumed alcohol. Exclusion criteria included significant weight change prior to participation, endocrine disorder (e.g., type 2 diabetes) or syndromic obesity. Parental informed consent and child assent were obtained from all participants before participation.

Participants underwent a complete physical examination and medical history by a certified nurse practitioner. Participants self-identified as black or white and pubertal development was assessed according to Tanner criteria (14). The study was approved by the University of Pittsburgh Institutional Review Board.

Anthropometric measurements were taken by trained research staff at the Pediatric Clinical and Translational Research Center. Body weight was measured to the nearest 0.1 kg and height was measured to the nearest 0.1 cm. Waist circumference was measured immediately below the last rib at the end of expiration and the average of two measures was used in the analyses. Total fat and fat free mass (FFM) was assessed using lunar iDXA (GE Healthcare,

Madison, WI, USA), visceral fat and abdominal subcutaneous adipose tissue (ASAT) at L4L5 was quantified using MRI (Siemens, Tim Trio, Erlangen, Germany) (10).

Liver fat was measured by proton magnetic resonance spectroscopy (^{1}H-MRS) with a 3T MR system (Siemens, Tim Trio, Erlangen, Germany) using a body matrix coil and a spine matrix using our established protocol (10). Fatty liver was defined as having liver fat [(methylene lipid peak/methylene lipid peak + water peak) X 100] ≥5% as shown previously (15). A fasting blood sample was obtained after an overnight fast (minimum 8 hours) to analyze liver enzymes [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)]. ALT and AST was not measured in one black boy whose liver fat was <5%. CRF was measured using a maximal graded treadmill test with the use of standard open-circuit spirometry techniques until volitional fatigue using our standard protocol (10).

Data are presented as means ± SD. Racial differences in participant characteristics were assessed using independent *t*-tests and chi-square tests. The associations between liver fat and anthropometric, body composition and CRF measures were examined with partial correlations adjusting for age and race. General linear modelling with least squared adjusted means was used to examine racial differences in liver fat adjusting for age and anthropometric, body composition or CRF measures. Independent associations with liver fat were determined with a second model with age, race, total fat, total FFM, visceral fat, ASAT and CRF. Logistic regression was used to assess the simple and independent associations between fatty liver and the body composition factors and CRF adjusting for age and race. Statistical analyses were performed using SAS v9.3 (NC, USA) with significance set at alpha ≤0.05.

RESULTS

In blacks, five out of 31 boys had liver fat ≥5% with three of the five boys with fatty liver also having an AST/ALT ratio <1. In whites, eight out of 26 boys had liver fat ≥5% with all eight having an AST/ALT ratio <1. White boys with fatty liver had a significantly higher BMI, waist circumference and visceral fat than white boys without fatty liver (P<0.05), while black boys had no significant differences in body composition (Table 1). White and black boys with fatty liver had higher ALT (P<0.05), but only white boys had significant differences in AST/ALT ratio (P=0.007).

Liver fat was associated (P≤0.05) with BMI percentile (r=0.28), total fat (r=0.31), waist circumference (r=0.38), visceral fat (r=0.62), ASAT (r=0.30), and CRF (r= −0.27) adjusting for age and race. White boys had greater liver fat than black boys with adjustment for age and differences in BMI percentile or CRF (Figure 1), but not with waist circumference, ASAT or visceral fat (P>0.05).

The independent associations of total and abdominal fat, and cardiorespiratory fitness to fatty liver is shown in Table 2. There were no racial differences in the odds of having fatty liver after adjusting for age and the body composition factors. Only waist circumference and visceral fat were associated with a higher odds of fatty liver (P<0.05). In a model with age, ethnicity, total body fat, total FFM, visceral fat, ASAT and CRF, only visceral fat was

independently associated with increased odds of having fatty liver (OR= 1.12, 95% CI: 1.04–1.21, *P*=0.003).

DISCUSSION

The present study demonstrated that visceral fat is significantly associated with liver fat and the odds of fatty liver in both obese black and white adolescent boys, and that the racial differences in liver fat were abolished after adjusting for the differences in the amount of visceral fat. These findings suggest that the racial differences in the level of visceral fat explains, in part, the observed differences in liver fat content between obese black versus white boys.

In the present study, adjusting for differences in BMI percentile and CRF failed to eliminate racial differences in liver fat between black versus white boys. Our findings are similar to the findings in adults (16) where racial differences in liver fat measured by ^{1}H-MRS between large samples of African-American, Caucasian and Hispanic adults were completely eliminated after adjusting for the differences in visceral fat, but not after adjusting for total fat and ASAT. Together, these observations may suggest that the same mechanisms that protect black youth from visceral fat accumulation may also protect them from liver fat accumulation despite having similar overall total body fat as compared to their white peers.

It has been suggested that the prevalence of a variant gene PNPLA3 expressed in liver is strongly associated with increasing liver fat and may also explain the observed racial differences in NAFLD in both adult (17) and pediatric (18) populations. Indeed, Santoro et al. (18) have reported a higher frequency of the PNPLA3 (rs738409) G allele in Hispanic (0.483) and Caucasian (0.324) obese children and adolescents, the groups had 66% and 41% prevalence of NAFLD compared with African-American youth (0.183), the group had the lowest (23%) prevalence of NAFLD. That the association between PNPLA3 (rs738409) G allele and liver fat were independent of BMI, visceral fat and glucose tolerance status in both African-American and Caucasian youth may suggest an important role of the PNPLA3 (rs738409) single nucleotide polymorphism in the development of early onset of NAFLD and explain the racial differences in NAFLD in obese African-American and Caucasian youth (18).

Strengths and limitations of this study warrant mention. First, although girls were present in the original studies, we were unable to include them since fatty liver was not present in our 63 obese black girls. Further, as this is a cross-sectional study we cannot infer causality and are unsure of the pathogenesis of NAFLD in relation with the development of visceral obesity. Finally, diet and physical activity have been shown to influence fatty liver, but as our sample was asked to keep a eucaloric normal fat diet (30%) and was sedentary at measurement, it is less likely that these factors influenced the observations here.

In conclusion, visceral fat is associated with an increased propensity to non-alcoholic fatty liver independent of race, and the racial disparities in liver fat between obese black versus white obese are explained, in part, by the differences in visceral fat.

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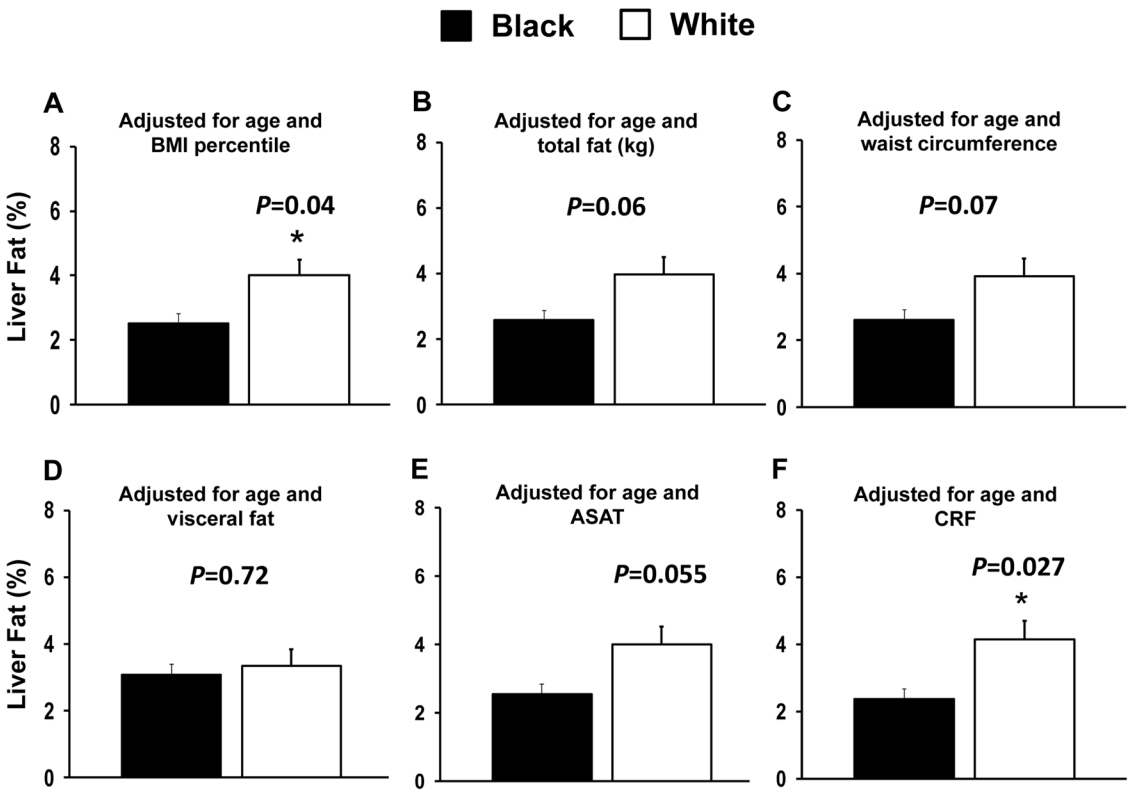

Figure 1.

Racial differences in the least squared adjusted means for liver fat (%) adjusted for age and A. BMI percentile, B. total fat (kg), C. waist circumference, D. visceral fat, E. ASAT (abdominal subcutaneous adipose tissue) and F. CRF (cardiorespiratory fitness).

TABLE 1

Descriptive characteristics in obese black and white boys with and without fatty liver

	Black			White		
	Fatty Liver absent (*n*=26)	**Fatty Liver present (*n*=5)**	***P***	**Fatty Liver absent (*n*=18)**	**Fatty Liver present (*n*=8)**	***P***
Age (years)	15.1 ± 1.7	14.4 ± 2.1	0.413	14.3 ± 1.5	15.1 ± 1.4	0.178
Tanner stage						
II–III/IV–V (*n*)	5/21	2/3	0.562	7/11	1/7	0.360
Height (cm)	171.5 ± 8.0	167.5 ± 11.9	0.352	173.0 ± 9.2	172.8 ± 6.7	0.966
BMI (kg/m^2)	34.8 ± 5.0	38.1 ± 3.3	0.163	32.2 ± 4.3	36.5 ± 5.7	0.048
BMI (percentile)	98.8 ± 1.1	99.5 ± 0.2	0.135	97.9 ± 3.2	99.2 ± 0.4	0.262
Waist circumference (cm)	102.4 ± 12.4	106.0 ± 7.2	0.532	98.7 ± 10.5	108.6 ± 8.6	0.027
Liver fat (%)	1.6 ± 1.1	7.9 ± 1.3	<0.001	2.1 ± 1.2	7.9 ± 2.0	<0.001
ALT (IU/l) *	21.8 ± 9.4	31.2 ± 9.0	0.049	21.3 ± 5.9	31.6 ± 6.6	0.001
AST (IU/l) *	26.4 ± 8.2	28.4 ± 7.1	0.611	23.9 ± 3.8	24.4 ± 3.9	0.767
AST/ALT ratio	1.3 ± 0.4	1.0 ± 0.3	0.062	1.2 ± 0.4	0.8 ± 0.1	0.007
Total fat (kg)	41.8 ± 12.0	46.5 ± 9.8	0.424	38.7 ± 9.4	45.7 ± 10.5	0.105
Total body fat (%)	40.4 ± 6.4	43.2 ± 6.3	0.382	39.9 ± 5.4	42.2 ± 6.0	0.349
FFM (kg)	60.4 ± 10.1	61.9 ± 16.5	0.793	57.9 ± 10.8	62.2 ± 9.9	0.341
Visceral fat (cm^2)	65.7 ± 27.8	88.9 ± 21.5	0.089	74.3 ± 20.2	116.4 ± 25.1	<0.001
ASAT (cm^2)	487.1 ± 163.9	548.6 ± 146.2	0.441	431.1 ± 124.1	535.4 ± 178.9	0.097
CRF (ml/kg/min) *	26.9 ± 6.1	24.2 ± 5.2	0.368	30.3 ± 5.1	26.8 ± 4.1	0.107

Mean ± SD. Fatty liver is defined as having liver fat ≥5% by ^{1}H-MRS.

WC, waist circumference; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

FFM, fat free mass; ASAT, abdominal subcutaneous adipose tissue; CRF, cardiorespiratory fitness.

*n=25 in black without fatty liver group.

TABLE 2

Independent associations of total and abdominal fat, and cardiorespiratory fitness to fatty liver

Variables	ORs	95% CI	*P*-values
BMI (percentile)	3.63	0.91 – 14.56	0.069
Waist circumference (cm)	1.08	1.0 – 1.16	0.049
Total fat (kg)	1.06	0.99 – 1.13	0.111
Total body fat (%)	1.08	0.96 – 1.22	0.198
FFM (kg)	1.05	0.96 – 1.14	0.309
Visceral fat (cm^2)	1.05	1.02 – 1.08	0.001
ASAT (cm^2)	1.00	1.0 – 1.01	0.112
CRF (ml/kg/min)	0.92	0.82 – 1.03	0.160

All models were adjusted for age.

Fatty liver is defined as having liver fat ≥5% by ^{1}H-MRS.

FFM, fat free mass; ASAT, abdominal subcutaneous adipose tissue; CRF, cardiorespiratory fitness.