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Pregnancy during adolescence has lasting adverse effects on blood lipids: A 10-year longitudinal study of black and white females

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BACKGROUND: Primiparity has been associated with 3 to 4 mg/dL lower high-density lipoprotein cholesterol concentrations in black and white adult women that persist several years after delivery.

OBJECTIVE: To examine the lasting effects of adolescent pregnancy on blood lipids, an early risk factor for future cardiometabolic diseases.

DESIGN: The National Heart Lung and Blood Institute's Growth and Health Study is a multicenter prospective cohort that measured fasting blood lipids for 1013 (513 black, 500 white) participants at baseline (1987–1988) ages 9–10, and again at follow-up (1996–1997) ages 18–19.

METHODS: Change in fasting plasma total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol, defined as the difference between baseline and follow-up measurements, was compared among 186 (145 black, 41 white) primi- or multiparas, 106 (55 black, 51 white) nulliparous, gravidas versus 721 (313 black, 408 white) nulligravidas. Fully adjusted multiple linear regression models estimated blood lipid changes among these pregnancy groups adjusted for race, age at menarche, baseline lipids, physical inactivity, body mass index, and family sociodemographics.

RESULTS: In the 10-year study period, adolescent paras compared with nulligravidas had greater decrements in high-density lipoprotein cholesterol (mg/dL; fully adjusted mean [95% confidence interval] group differences in black −4.3 [−6.7, −2.0]; $P < .001$ and white: −4.5 [−8.2, −0.7]; $P = .016$) and greater increments in fasting triglycerides (mg/dL; adjusted mean [95% confidence interval] group differences in black: 10.4 [3.9, 16.8]; $P < .001$, and white: 11.6 [−3.6, 26.8]; $P = .167$).

CONCLUSION: Adolescent pregnancy contributes to pro-atherogenic lipid profiles that persist after delivery. Further research is needed to assess whether adolescent pregnancy has implications for future cardiovascular disease risk in young women.

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Parity is associated with lower plasma high-density lipoprotein cholesterol (HDL-C) in mid- to late life. Yet, evidence from cross-sectional studies is mixed; some report lower HDL-C among grand multiparas and multigravidas (five or more births or pregnancies),[1,2] and others report a graded linear inverse association.[3–5] By contrast, longitudinal studies from before to after pregnancy observed lower HDL-C after a first birth (primiparity) compared with never giving birth (nulliparity) or becoming pregnant (nulligravidity).[6,7] The mixed findings imply that the impact of parity on HDL-C may depend on the life stage, sociodemographics, or other determinants of parity, as well as limitations in study design.

The authors of cross-sectional studies, conducted in primarily postmenopausal women, reported 4 to 5 mg/dL lower HDL-C associated with greater parity or gravidity (ie, ≥5 births versus ≤4 births, and 6–8 pregnancies vs 0 pregnancies, respectively),[1,2] as well as a graded inverse association with the number of births.[3–5,8] These studies are limited by the lack of prepregnancy blood lipid measurements and retrospective assessment of other risk factors within decades after the childbearing years.

Longitudinal studies of women of reproductive age (18–30 years) based on the Coronary Artery Risk Development in Young Adults (CARDIA) study are unique because measurements of fasting lipids were obtained both before and after pregnancy. In CARDIA, a lower mean HDL-C of 3 to 4 mg/dL was found among primiparas compared with nulligravidas up to 8 years after delivery.[7] Moreover, the persistent decrement in HDL-C did not increase with the number of births (ie, similar magnitude of the decrement in HDL-C for primiparas and multiparas). The findings persisted after adjustment for race, prepregnancy body mass index (BMI) and HDL-C, smoking habit, and sociodemographics as well changes in body weight, waist girth, alcohol intake, and physical activity.[7] These longitudinal data support the hypothesis that a first pregnancy is associated with lasting biologic effects on maternal metabolism.

Adolescence is a critical period for development of cardiovascular disease (CVD) risk factors, including the predisposition to obesity.[9–11] Blood lipid changes during adolescence coincide with hormonal changes related to the onset of puberty, including decreased total cholesterol and increased triglyceride concentrations.[12–14] Excessive weight gain during adolescence could be particularly harmful because of enhanced abdominal fat deposition,[15] a strong predictor of future dyslipidemia and insulin resistance.[16]

Pregnancy during adolescence may have persistent adverse effects on future cardiometabolic disease risk. Specifically, pregnant adolescents are more likely than pregnant adults to experience excessive gestational weight gains[17,18] and substantial postpartum weight retention.[19] In the National Heart Lung and Blood Institute's Growth and Health Study (NGHS), parous compared with nulligravid adolescents gained more weight and had greater increased in waist circumference after pregnancies.[20] Thus, adolescent pregnancy may contribute to obesity onset and more atherogenic blood lipids that increase CVD risk later in life.

We sought to determine whether pregnancy has lasting adverse effects on blood lipids among parous (1 or more births) compared with nulligravid (never pregnant) adolescents within the NGHS, a multicenter, biracial (50% black) cohort of young females in which blood lipids were measured at ages 9–10 years and again at 18–19 years. In the 10-year NGHS, one-third of participants became pregnant during adolescence. The NGHS provides a unique opportunity to examine the natural history of pregnancy during adolescence and its effects on changes in maternal blood lipids within this key developmental period. The prospective cohort design and internal comparison group of nulligravid adolescents allow us to examine the persistent effects of pregnancy on blood lipids (i.e., months to years after delivery) apart from other risk factors, including prepregnancy lipids.

Methods

Study participants

The NGHS is a 10-year longitudinal observational investigation of the etiologic factors related to the development of risk factors for cardiovascular disease, including obesity, in a cohort of black and white girls examined annually from childhood (age 9–10 years) up to age 19 years.[21,22] Details of cohort recruitment, characteristics, study methods, and instruments are described elsewhere.[21–23] To summarize in brief, participants were recruited between January 1987 and May 1988 from three centers: (1) University of California at Berkeley, (2) University of Cincinnati Medical Center and Children's Hospital Medical Center, and (3) Westat, Inc, in Rockville, Maryland. Participants were recruited by the University of California at Berkeley via census sampling from all public and parochial schools in west Contra Costa County, California, and by the University of Cincinnati/Cincinnati Children's Hospital Medical Center from public and parochial schools that were racially and socioeconomically representative of the greater Cincinnati area in Ohio. Westat Inc. recruited participants from Group Health Association, a health maintenance organization in the Washington, DC, area. Institutional review boards at each participating study center approved the study. Written, informed consent was obtained from subjects and their parents or guardians for all study procedures.

In 1987–1988, 2379 girls aged 9–10 years (1213 black, 1166 white) and their families were enrolled, and 2094 were re-examined at age 18–19 in 1997–1998 (88% retention). Of 2094 girls, 471 reported one or more births (primi- or multiparas), 224 reported one or more pregnancies but no births (gravidas who are nulliparous), 84 were missing reproductive history, and 1315 girls reported no pregnancies (nulligravidas) during the NGHS study period. We selected participants who reported pregnancies or

births, or had incomplete information on reproductive history (n = 779) for the NGHS Pregnancy study (2002–2005), in which telephone interviews were performed to confirm pregnancies and births during the NGHS study period. We also requested permission to abstract pregnancy medical records and to obtain copies of their children's birth certificates. To evaluate completeness or reporting, we used data collected (ie, birthdates for their infants) from NGHS Wave-II (n = 2054) in 1998–2001 to ascertain whether additional births had occurred that had not been reported during the NGHS study period.[24] For parous adolescents, visits were scheduled at least 4 months postpartum.

For this analysis we selected 1013 participants (531 black, 500 white; 43% of the original cohort) who had provided fasting blood specimens analyzed for lipids at both enrollment (1987–1988) and follow-up examinations (1997–1998), triglycerides ≤400 mg/dL (1 person excluded), as well as pregnancy history during the NGHS study period. All pregnancies for this sample occurred within the 10-year period between the two NGHS examinations. Among 1013 adolescents, 186 (145 black, 41 white) experienced one or more births (38 multiparas), 106 were pregnant but did not give birth, and 721 were never pregnant during the NGHS study period. Participants not included were more likely to have enrolled in the Cincinnati, Ohio, site and to have parents with less education, and lower family incomes ($P < .01$) than the analytic sample.

Data collection

Plasma lipid profiles

Blood specimens were collected in the morning after a 12-hour overnight fast. Total and HDL-cholesterol were determined using the Cholesterol CHODPAP method (Bochringer–Mannheim diagnostics). Blood triglycerides were analyzed enzymatically with the use of a commercially available method (Abbott A-Gent Triglycerides Reagent Set). Quantitative assays of blood lipids were performed at the John Hopkins University's Lipoprotein Analytic Laboratory, a participant in the Centers for Disease Control NHLBI Lipid Standardization Program. Low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald formula: LDL-cholesterol = total cholesterol – HDL-cholesterol – (triglycerides/5). Lipid changes were calculated as the difference between visit 10 (1997–1998) and baseline (1987–1988) measurements to ensure consistency of lipid measures before menarche and because lipids were not measured at each examination. Because LDL-C could not be calculated for triglycerides greater 400 mg/dL, we excluded 1 participant at follow-up (age 18–19 years). Participants who reported any pregnancies were scheduled for the follow-up examination at least 4 months after the pregnancy ended.

Anthropometric measures

Body weight was measured to the nearest 0.1 kg with calibrated Healtho-meter electronic scales (Model 482, Sunbeam Products, Inc, Maitland, FL) and participants wearing only a paper hospital gown or large NGHS standard t-shirt. Two weight measurements were obtained and a third was taken if the first two differed by more than 0.3 kg. Height was measured to the nearest 0.1 cm in socks, using custom-made portable stadiometers. A third measurement was taken if the first two were more than 0.5 cm apart.[21]

Reproductive history

Participants were asked if they had ever been pregnant, were currently pregnant, number of times they had been pregnant, number of births and birth dates of their children annually from visit 6 (age 14–15;1990–1991) through visit 10 (age 18–19;1997–1998). A birth was defined as a live or still birth, abortion, or fetal death for any pregnancy lasting 20 weeks or more that was delivered at least 4 months before visit 10. A pregnancy that did not end in a birth was defined as a spontaneous or therapeutic abortion, ectopic or molar pregnancy, or miscarriage < 20 weeks gestation. The Pregnancy study conducted in 2002–2004 and the NGHS Wave-II from 1998 to 2001 augmented information on pregnancies and births.

Participants were classified as: 1) primi- or multiparous, 2) gravid and nulliparous, or 3) nulligravida. Among parous adolescents, we calculated age at first delivery and dichotomized them as less than 16, or ≥16 years at first delivery.

Other covariates

Age at menarche (maturation stage) and hormonal contraceptive use

Annually, participants were asked if they had started their menstrual cycles. Thus, age at menarche was determined from participants' self-declaration. Questions about oral contraceptive use were asked annually starting at visit 3 (age 11–12). Questions on Norplant and Depo-provera were added to the questionnaires at visits 9 and 10 (ages 17–19) when the contraceptive products came on the market. We categorized girls as never, past, or current users of hormonal contraceptives at the last NGHS visit. Current users at ages 18–19 were classified by type of hormonal contraceptives (ie, oral or Norplant/Depo-provera).

Sociodemographic, familial, and lifestyle attributes

Parents and guardians provided information on race, age, family composition, maximum parental education, employment, and household income at the baseline examination. Girls provided information on dietary intake and physical activity patterns annually. Methods for collecting dietary intake and physical activity information were validated by the use of actual observed eating and activity behavior as previously described.[25] The 3-day food record was selected due to greater accuracy than 24-hour recall or 5-day food frequency methodologies.[26] The Nutrition

Coordinating Center at the University of Minnesota and the Cincinnati Children's Hospital Medical Center coded the food records from years 1 and 10, respectively, including number of meals and snacks, and estimated nutrients using Version 11 of the Nutrition Coordinating Center nutrient database as detailed elsewhere.[21] The nutrition questionnaire also asked participants about their frequency of eating fast foods, and dieting to lose weight.

Physical activity was self-reported via questionnaire and a 3-day diary for the same period as the diet was recorded. The participants were asked to respond to the following statement, "I am physically active, that means I get lots of exercise", by choosing from among one of three responses: "never or almost never;" "sometimes;" "usually or always." Self-perception of physical activity responses were dichotomized with the "never or almost never" response as the referent, and "sometimes" and "usually or always" responses combined into another group. A measure of sedentary behavior, girls reported the number of hours of television or video watched per week. Methodology to collect physical activity data and quantify the scores has been previously described.[27] If dietary intake or physical activity was missing at baseline ($n = 70$), we used data from the next available visit up to year 4.

Statistical analysis

Baseline differences in characteristics of participants and their parents were described by race using chi-square statistics for categorical variables (clinic site, household income, parental education, BMI) and by comparison of means for continuous variables using *t*-tests (fasting plasma lipids, age, height, dietary intake, television and video viewing, and age at menarche). Bivariate associations between race and reproductive characteristics at the end of follow–up were also examined by the use of *t*-tests and chi-square statistics. Within each race, blood lipids, age at menarche, height at age 18–19 years, and hormonal contraceptive use categories were examined across pregnancy groups using F-statistics from analysis of variance. Blood lipids were similar for primi- and multiparas, and because few adolescents gave birth two or more times ($n = 38$; 4 white, 34 black), we combined them into one group (one or more births; parous) for each race. All *P*-values presented are for two-sided tests; statistical significance was defined to be $P < .05$.

Unadjusted and multivariable adjusted means (95% confidence intervals [CI]) and mean group differences in plasma lipid changes among pregnancy groups were estimated from linear regression models. Statistically significant *P* values and confidence intervals were corrected for multiple comparisons of paras or nulliparas to nulligravidas using the Dunnett's procedure in SAS for Windows 9.1.3 (SAS Institute Inc., Cary, NC). Covariates evaluated as potential confounders based on *a priori* hypotheses included race, baseline measurements, age at menarche, parental education, household income, height at age 18–19 years, and lifestyle behaviors (baseline physical activity and dietary patterns). Covariates were excluded as confounders if they were not associated with the dependent variables independent of the other covariates. Effect modification by race within pregnancy group associations for each lipid was evaluated by introduction of appropriate cross-product terms into the models (significance $P < .10$). Adjusted least square means for fasting lipid changes among pregnancy groups (nulligravida, referent) were obtained from race-specific linear regression models.

We examined mean plasma lipid changes stratified by race because of the small number of parous White adolescents that limited statistical power to detect effect modification. We also obtained the race-specific results for this study so that our findings could be compared with previous study findings in adults (black and white) reporting race-specific longitudinal changes in plasma lipids (from before to after pregnancy) associated with parity.

Fully adjusted means (95% CI) for changes in fasting lipids among pregnancy groups were adjusted for the relevant baseline plasma lipid measurement, age, weight, and height (BMI) at age 9–10, clinic, age at menarche, parental education, household income, and physical inactivity. Height at age 18–19 years did not affect pregnancy group estimates of lipid changes.

We examined BMI change and hormonal contraceptive use as potential mediators of the pregnancy association with blood lipid changes. Giving birth during adolescence was associated with use of progesterone only contraception (Depo-provera/Norplant) at follow-up; 25% to 35% of parous versus fewer than 11% of nonparous adolescents. To assess the effects of pregnancy without exposure to progesterone-only hormonal contraception, we also conducted a sensitivity analysis that excluded 89 adolescents using Depo-provera or Norplant.

Results

Baseline characteristics that varied by race include lower parental education and income, lower fasting plasma triglycerides, greater fasting plasma HDL-C, body weight, height, dietary intake (Kcal as fat), and physical inactivity and greater percentages of overweight and obesity among black versus white girls. Age at menarche was 10 months later on average for white versus black girls ($P < .001$; Table 1). Reproductive status varied by race (Table 2); black compared with white adolescents were more likely to become pregnant and/or give birth (28% vs 8% respectively; $P < .001$) and more likely to be currently using Norplant or Depo-provera in 1997–1998 ($P < .001$).

Baseline and follow-up blood lipids, and BMI were mostly similar by subsequent number of pregnancies and births during adolescence (Table 3). However, black primi- or multiparas had lower plasma HDL-C and greater triglycerides at follow-up than nulligravidas. Among white subjects, primiparas had the greatest mean BMI at follow-up. Age at menarche did not differ by pregnancy groups

Table 1 Characteristics at age 9–10 years (baseline, 1987–1988) and age at menarche by race

Characteristics at age 9–10 years	Black n = 513	White n = 500	*P* value
Annual household (family) income	*n (%)*		<.001
<$20,000	211 (41.1)	68 (13.6)	
$20,000–$50,000	212 (41.3)	236 (47.2)	
>$50,000	90 (17.5)	196 (39.2)	
Parental education			<.001
High school or less	140 (27.3)	75 (15.0)	
Post-high school/some college	258 (50.3)	154 (30.8)	
Four or more years of college	115 (22.4)	271 (54.2)	
Study Site			.003
Berkeley, CA	197 (38.4)	232 (46.4)	
Cincinnati, OH	129 (25.2)	135 (27.0)	
Washington, DC	187 (36.5)	133 (26.6)	
Body size, BMI kg/m^2			<.001
Overweight (>95th)	94 (18.3)	37 (7.4)	
At risk for overweight (85th to 95th)	82 (16.0)	68 (13.6)	
Normal (<85th)	337 (65.7)	395 (79.0)	
	Mean (SD)		
Fasting plasma lipids, mg/dL			
HDL-C	55.9 (13.3)	53.5 (11.2)	.002
LDL-C	104.1 (28.7)	104.7 (26.0)	.77
Total cholesterol	170.9 (30.8)	170.2 (26.6)	.70
Triglycerides	70.8 (32.4)	78.6 (34.6)	<.001
Height, cm	143.4 (7.9)	139.6 (7.1)	<.001
Weight, kg	40.2 (11.3)	35.0 (8.2)	<.001
Dietary intake*			
Total Kcal	1907.6 (629.3)	1806.2 (444.3)	.003
Fiber g/day	11.6 (5.1)	11.6 (4.5)	.98
% Kcal as fat	2.1 (0.8)	2.1 (0.6)	.14
Physical inactivity†	36.5 (17.7)	24.9 (14.8)	<.001
Video/television viewing (hrs/week)			
Age at menarche (yrs)	12.0 (1.1)	12.8 (1.2)	<.001

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
*Dietary intake at baseline or years 2, 3, or 4. Missing dietary intake: n = 1 white and n = 1 black.
†Video/television viewing at baseline or the next available year.

for the black NGHS participants, but white nulligravidas reached menarche at slightly older ages. Overall, pregnancy groups in both races differed in hormonal contraceptive use ($P < .001$). Paras were more likely to be past or current users of hormonal contraceptives, including Norplant or Depo-provera at follow-up ($P < .001$). Height differences were significant among paras versus nulligravidas at baseline among black adolescents and at follow-up among white adolescents. We combined primiparas and multiparas together within each race group for multivariable analyses because of the very small numbers of multiparas in each race group.

In multivariable models, there was no evidence of effect modification by race (Table 4) in the association of pregnancy groups with change in fasting lipids; all race interactions $P > .25$, although our power was limited due to the small number of parous whites. We describe lipid changes stratified by race to describe within race characteristics of blood lipids related to parity and gravidity because of the much smaller sample of parous white participants.

Unadjusted mean (95% CI) changes in fasting lipids during the 10-year period were similar among pregnancy groups, except for lower HDL-C and greater triglycerides in primi- or multiparas than nulligravidas. In black and white races, respectively, unadjusted mean group differences in HDL-C were −4.2 mg/dL lower ($P = .002$) and −4.1 mg/dL ($P = .044$) lower in paras than nulligravidas. Triglyceride mean group differences from unadjusted models were 12.0 mg/dL greater among black primi- or multiparas ($P = .003$), and 13.0 mg/dL greater ($P = .127$) among white primi- or multiparas than nulligravidas for specific race groups.

In multivariable models fully adjusted for covariates (age, clinic sites, family income, parental education, age at menarche, baseline lipid measurement, BMI at age 9–10, and physical inactivity), mean group differences in HDL-C were slightly greater; − 4.3 mg/dL (−6.7 to −2.0) and −4.5 mg/dL (−8.2 to −0.7) for parous black and white adolescents, respectively, ($P < .001$ and .016). Mean group differences for fasting triglycerides were attenuated to

Table 2 Pregnancy groups and hormonal contraceptive use during the NGHS study period (1987–1997) by race, n (%) or mean (SD), n = 1013

Characteristics at age 18–19 years, n (%)	Black *n* = 513	White *n* = 500	*P* value
Pregnancy groups			<.001
Nulligravid	313 (61.0)	408 (81.6)	
Gravid, nulliparous	55 (10.7)	51 (10.2)	
Primi- or multiparous: 1 or more births	145 (28.3)	41 (8.2)	
Number of births:			.055
1 birth	111 (76.6)	37 (90.2)	
2 or more births	34 (23.4)	4 (9.8)	
Age at first birth*			.45
<16 yrs	32 (22.5)	7 (17.1)	
≥16 yrs	110 (77.5)	34 (92.9)	
Hormonal contraceptive use			<.001
Never	266 (51.9)	262 (52.4)	
Past	91 (17.7)	63 (12.6)	
Current oral contraceptives	93 (18.1)	149 (29.8)	
Current Depo-provera or Norplant	63 (12.3)	26 (5.2)	

NGHS, National Heart Lung and Blood Institute Growth and Health Study.
*Age at first birth missing; black n = 3.

10.4 mg/dL (3.9–16.8) and 11.6 (–3.6 to 26.8), respectively, for black and white paras ($P < .001$ and .167). Adjustment for BMI change moderately attenuated pregnancy group differences in blood lipids, but HDL-C remained significantly lower for black ($P = .010$) and white paras ($P = .018$). Triglycerides increments were also attenuated but remained significant for black paras versus nulligravidas ($P = .030$). Finally, Norplant, Depo-provera or other hormonal contraceptive use attenuated mean pregnancy group differences in HDL-C among black ($P = .033$) and white girls ($P = .124$) but had minimal impact on triglyceride changes. In the sensitivity analysis where progesterone only users were excluded, results (data not shown) remained similar to those for the full sample. There was no evidence for differences in LDL-C, or total cholesterol changes among pregnancy groups in fully adjusted multivariable models. Among paras within race groups, associations did not vary by age at first birth.

Discussion

Our study findings show that both black and white parous adolescents experienced greater decrements in HDL-C (4.3–4.5 mg/dL) and greater increments in fasting triglycerides (10.4–11.6 mg/dL) after pregnancy compared with lipid changes for nulligravid adolescents during the same 10-year study period. These differences in HDL-C and triglycerides for parous adolescents remained significant after adjustment for BMI and lipid measurements at age 9–10 years, age at menarche, family sociodemographics, and lifestyle behaviors, except for triglycerides in white adolescents. The strength of these associations was similar among black and white adolescents, despite fewer pregnancies in white girls.

Excess weight gain and increased use of hormonal contraception after pregnancy appeared to modestly mediate the association between adolescent pregnancy and proatherogenic lipid profiles, primarily for attenuation of differences in HDL-C among the black adolescents. Yet, both HDL-C and triglyceride differences among parous versus nulligravid participants remained statistically significant after controlling for change in BMI, except for triglyceride differences among white girls. Our sensitivity analysis, in which we excluded hormonal contraceptive users, showed that our findings remained robust among participants never using hormonal contraceptives.

Our mean concentrations for LDL-C and total cholesterol in the NGHS are comparable with national estimates for LDL-C and total cholesterol, respectively, in adolescent females aged 12–17 years; 93.5 mg/dL and 165.9 mg/dL for black, and 89.8 mg/dL and 165.4 mg/dL for white.[28] Another longitudinal study of lipid changes in females (20% black) followed from age 9 to 18 years reported total cholesterol decrements of 19 mg/dL and triglycerides increments of 15 mg/dL but did not report whether the adolescents had given birth.[13] The lipid changes observed within the NGHS cohort are consistent with the previous study, particularly for the white females, but NGHS black females showed modest decrements in fasting triglycerides.

Our finding that a first birth is associated with lower mean HDL-C that persists after pregnancy independent of weight gain among adolescents is consistent with previous findings for adult women. CARDIA reported that primiparity compared with nulligravidity was associated with 3 to 4 mg/dL lower plasma HDL-C within 2 to 8 years after delivery among both black women and white women aged 20–31 years.[6,7] The HDL-C decrements in CARDIA women persisted after the first birth, and were not greater

Table 3 Participant characteristics at baseline and follow–up among pregnancy groups by race; mean (SD) or *n* (%), (NGHS 1987–1997)

Characteristics	Pregnancy groups				
White race	Nulligravidas *n* = 408	Gravid, Nulliparas *n* = 51	Primiparas *n* = 37	Multiparas *n* = 4	*P* value
Baseline age 9–10 yr:					
BMI, kg/m^2	17.7 (3.2)	18.2 (2.8)	18.6 (3.2)	17.4 (1.9)	.32
Height, cm	139.5 (7.1)	140.6 (7.7)	139.0 (6.7)	139.1 (6.9)	.71
HDL–C, mg/dL	53.6 (11.4)	53.0 (11.7)	52.9 (7.7)	58.3 (6.2)	.81
LDL–C, mg/dL	104.6 (25.7)	104.8 (31.4)	104.4 (22.5)	109.8 (12.8)	.98
Total cholesterol, mg/dL	170.3 (26.1)	169.5 (34.2)	169.0 (20.8)	179.8 (19.8)	.89
Triglycerides, mg/dL	79.1 (35.3)	76.0 (31.9)	76.7 (32.7)	75.5 (25.6)	.91
Follow-up† age 18–19 yr					
BMI, kg/m^2	23.6 (4.9)	23.2 (4.4)	26.0 (6.6)	21.9 (1.9)	.03
Height, cm	165.9 (6.3)	164.0 (6.7)	162.9 (6.0)	161.2 (9.1)	.01
HDL-C, mg/dL	52.8 (10.7)	53.5 (15.4)	48.1 (8.1)	53.5 (14.6)	.08
LDL-C, mg/dL	98.8 (29.8)	98.4 (29.1)	107.7 (35.4)	103.0 (30.9)	.38
Total cholesterol, mg/dL	165.7 (32.4)	165.1 (32.6)	172.0 (37.8)	167.5 (28.6)	.73
Triglycerides, mg/dL	91.9 (40.7)	85.5 (33.1)	105.5 (47.2)	72.5 (48.5)	.10
Age at menarche, yr	12.8 (1.2)	12.5 (1.2)	12.3 (1.2)	12.3 (0.5)	.02
Hormonal contraceptives*					<.001
Never	249 (61.0)	10 (19.6)	2 (5.4)	1 (25.0)	
Past	37 (9.1)	14 (27.5)	11 (29.7)	1 (25.0)	
Current oral	112 (27.5)	22 (43.1)	14 (37.8)	1 (25.0)	
Norplant/Depo-Provera	10 (2.5)	5 (9.8)	10 (27.0)	1 (25.0)	

Characteristics	Pregnancy Groups				
Black race	Nulligravidas *n* = 313	Gravid, Nulliparas *n* = 55	Primiparas *n* = 111	Multiparas *n* = 34	*P* value
Baseline age 9–10 yr:					
BMI, kg/m^2	19.6 (4.5)	19.3 (4.2)	18.5 (3.3)	19.4 (4.2)	.11
Height, cm	143.5 (8,2)	143.0 (7.3)	142.2 (7.0)	147.5 (7.8)	0.007
HDL-C, mg/dL	55.4 (13.7)	59.1 (11.7)	55.7 (13.3)	55.5 (12.3)	.32
LDL-C, mg/dL	104.2 (28.1)	105.3 (31.9)	104.7 (28.4)	100.2 (30.3)	.85
Total cholesterol, mg/dL	170.7 (30.7)	174.6 (33.9)	171.1 (29.1)	166.3 (33.0)	.67
Triglycerides, mg/dL	72.2 (34.7)	67.0 (27.9)	68.9 (25.9)	69.4 (37.2)	.61
Follow-up† age 18–19 yr					
BMI, kg/m^2	26.9 (7.9)	26.2 (7.2)	27.2 (7.1)	30.4 (9.1)	.07
Height, cm	164.2 (6.3)	164.0 (6.2)	163.8 (6.1)	164.3 (6.4)	.92
HDL-C, mg/dL	55.8 (12.4)	54.9 (9.8)	51.9 (11.9)	51.8 (13.0)	.02
LDL-C, mg/dL	96.5 (27.0)	101.5 (32.1)	98.9 (28.6)	103.1 (38.8)	.42
Total cholesterol, mg/dL	162.5 (28.8)	166.4 (34.9)	162.1 (29.0)	167.2 (40.6)	.69
Triglycerides, mg/dL	66.9 (25.5)	65.6 (22.4)	74.4 (37.9)	79.8 (38.4)	.01
Age at menarche, yr	12.0 (1.1)	12.0 (1.2)	12.1 (1.1)	11.8 (1.2)	.48
Hormonal contraceptives*					<.001
Never	209 (66.8)	18 (32.7)	32 (28.8)	7 (20.6)	
Past	36 (11.5)	17 (30.9)	27 (24.3)	11 (32.4)	
Current oral	52 (16.6)	14 (25.5)	23 (20.7)	4 (11.8)	
Norplant/Depo-Provera	16 (5.1)	6 (10.9)	29 (26.1)	12 (35.3)	

BMI, body mass index; HDL-C, high-density lipoprotein; LDL-C, low-density lipoprotein; NGHS, National Heart Lung and Blood Institute Growth and Health Study.

*n(%).

†Fasting plasma lipids and lipoprotein cholesterol.

with subsequent births controlling for changes in weight and lifestyle behaviors (i.e., physical activity, alcohol intake).[7]

In contrast to CARDIA findings, parous adolescents in NGHS also showed greater fasting triglycerides than nulligravidas, although statistical significance was not reached

Table 4 Unadjusted and multivariable adjusted mean (95% CI) changes (Δ) in fasting plasma lipids (HDL-C, LDL-C, total cholesterol, and triglycerides) for pregnancy groups by race (NGHS, 1987–1997)

Change in lipids	Pregnancy groups, mean absolute change (Δ) in lipids (95%CI)			Overall Group $P^{\dagger}$	Mean group differences (95% CI) for paras versus nulligravidas	Pairwise comparison P
	Nulligravidas Blacks n =313, White n =408	Gravidas, nulliparas Black n = 55, White n = 51	Primi- or multiparas Black n = 145, White n = 41			
ΔHDL-C, mg/dL						
Black						
Unadjusted	0.3 (–1.0 to 1.7)	−4.2 (−7.5 to −0.9)	−3.8 (−5.8 to −1.8)	<.001	−4.2 (−6.9 to −1.4)**	.002
Fully adjusted	−0.5 (−1.8 to 0.7)	−3.6 (−6.3 to −0.8)	−4.9 (−6.7 to −3.1)	<.001	−4.3 (−6.7 to −2.0)***	<.001
Adjusted + ΔBMI, mediator	−1.0 (−2.2 to 0.2)	−4.1 (−6.8 to −1.4)	−3.9 (−5.7 to −2.2)	.006	−2.9 (−5.3 to −0.6)*	.010
Adjusted + HC, mediator	−1.9 (−3.4 to −0.5)	−4.2 (−6.9 to −1.4)	−4.7 (−6.4 to −2.9)	.041	−2.7 (−5.3 to −0.1)*	.033
White						
Unadjusted	−0.8 (−1.8 to 0.3)	0.5 (−2.4 to 3.5)	−4.8 (−8.2 to −1.5)	.043	−4.1 (−8.1 to −0.1)*	.044
Fully adjusted	−0.8 (−2.0 to 0.4)	−0.3 (−3.0 to 2.4)	−5.3 (−8.4 to −2.2)	.021	−4.5 (−8.2 to −0.7)*	.016
Adjusted + ΔBMI, mediator	−0.7 (−1.9 to 0.5)	−0.6 (−3.3 to 2.1)	−5.1 (−8.1 to −2.0)	.029	−4.4 (−8.1 to −0.6)*	.018
Adjusted + HC, mediator	−2.1 (−3.7 to −0.5)	−1.6 (−4.3 to 1.2)	−5.4 (−8.4 to −2.3)	.127	−3.2 (−7.1 to 0.7)	.124
ΔLDL-C, mg/dL						
Black						
Unadjusted	−7.7 (−10.4 to −5.0)	−3.8 (−10.4 to 2.6)	−3.8 (−7.8 to 0.2)	.214	3.9 (−1.6 to 9.4)	.211
Fully Adjusted	−7.6 (−10.2 to −4.9)	−2.5 (−8.5 to 3.5)	−3.5 (−7.5 to 0.3)	.111	3.9 (−1.2 to 9.1)	.162
Adjusted + ΔBMI, mediator	−6.5 (−9.1 to −4.0)	−1.2 (−7.0 to 4.5)	−5.6 (−9.4 to −1.8)	.227	0.9 (−4.1 to 5.9)	.901
Adjusted + HC, mediator	−6.0 (−9.2 to −2.9)	−2.0 (−8.0 to 4.0)	−3.3 (−7.2 to 0.6)	.350	2.7 (−2.8 to 8.2)	.460
White						
Unadjusted	−5.8 (−8.6 to −3.1)	−6.5 (−14.2 to 1.3)	2.4 (−6.2 to 11.0)	.195	8.2 (−2.1 to 18.5)	.145
Fully adjusted	−5.5 (−8.8 to −2.3)	−8.6 (−15.9 to −1.3)	−1.8 (−10.1 to 6.6)	.453	3.8 (−6.4 to 14.0)	.644
Adjusted + ΔBMI, mediator	−6.4 (−9.6 to −3.1)	−7.1 (−14.3 to 0.1)	−3.2 (−11.4 to 4.9)	.737	3.2 (−6.8 to 13.1)	.725
Adjusted + HC, mediator	−7.4 (−11.6 to −3.2)	−11.4 (−18.5 to −4.2)	−2.7 (−10.6 to 5.3)	.246	4.8 (−5.4 to 15.0)	.498
ΔTotal cholesterol, mg/dL						
Black						
Unadjusted	−8.2 (−11.0 to −5.3)	−8.2 (−15.0 to −1.4)	−6.6 (−10.8 to −2.5)	0.828	1.5 (−4.2 to 7.3)	.793
Fully adjusted	−8.6 (−11.4 to −5.9)	−6.7 (−12.9 to −0.5)	−7.1 (−11.2 to −3.1)	0.740	1.5 (−3.8 to 6.8)	.770
Adjusted + ΔBMI, mediator	−7.9 (−10.6 to −5.2)	−5.7 (−11.8 to 0.4)	−8.7 (−12.7 to −4.7)	0.714	− 0.8 (−6.1 to 4.5)	.928
Adjusted + HC, mediator	−8.5 (−11.8 to −5.3)	−7.0 (−13.1 to −0.8)	−6.5 (−10.5 to −2.5)	0.705	2.0 (−3.6 to 7.7)	.659
White						
Unadjusted	−4.6 (−7.5 to −1.7)	−4.4 (−12.6 to 3.8)	1.5 (−7.7 to 10.6)	0.459	6.1 (−4.9 to 17.1)	.380
Fully adjusted	−4.3 (−7.8 to −0.7)	−7.3 (−15.3 to 0.7)	−3.1 (−12.2 to 5.9)	0.732	1.2 (−9.9 to 12.2)	.966
Adjusted + ΔBMI, mediator	−5.2 (−8.7 to −1.7)	−5.6 (−13.5 to 2.2)	−4.7 (−13.6 to 4.1)	0.987	0.5 (−10.4 to 11.3)	.994
Adjusted + HC, mediator	−7.5 (−11.9 to −3.1)	−11.9 (−19.4 to −4.5)	−4.3 (−12.6 to 4.0)	0.345	3.2 (−7.5 to 13.9)	.748

ΔTriglycerides, mg/dL						
Black						
Unadjusted	−5.3 (−9.4 to −1.3)	−1.4 (−11.1 to 8.3)	6.6 (0.7 to 12.6)	0.005	12.0 (3.7 to 20.2)**	.003
Fully adjusted	−3.3 (−6.6 to 0.0)	−1.8 (−9.3 to 5.7)	7.0 (2.0 to 11.9)	0.002	10.4 (3.9 to 16.8)***	<.001
Adjusted + ΔBMI, mediator	−2.2 (−5.4 to 1.0)	−0.2 (−7.5 to 7.1)	4.8 (− 0.1 to 9.6)	0.053	6.9 (0.6 to 13.3)*	.030
Adjusted + HC, mediator	−3.2 (−7.1 to 0.7)	−2.8 (−10.2 to 4.7)	7.9 (3.1 to 12.7)	<.001	11.1 (4.2 to 17.9)***	<.001
White						
Unadjusted	12.8 (8.6 to 16.9)	9.5 (−2.2 to 21.3)	25.7 (12.6 to 38.9)	0.144	13.0 (−2.8 to 28.7)	.127
Fully adjusted	12.9 (8.1 to 17.8)	9.4 (−1.6 to 20.4)	24.5 (12.1 to 37.0)	0.151	11.6 (−3.6 to 26.8)	.167
Adjusted + ΔBMI, mediator	11.7 (6.9 to 16.4)	11.7 (1.0 to 22.4)	22.1 (10.0 to 34.3)	0.275	10.5 (−4.3 to 25.3)	.212
Adjusted + HC, mediator	12.1 (5.9 to 18.4)	4.7 (−5.9 to 15.3)	23.4 (11.6 to 35.1)	0.057	11.2 (−4.0 to 26.4)	.186

Fully adjusted models include covariates age, clinic site, household income, parental education, age at menarche, relevant baseline fasting blood lipid measurement, weight and height at age 9–10 (included as BMI), and physical inactivity.

Mediators of blood lipid changes: ΔBMI = change in body mass index (BMI), HC = hormonal contraceptive use.

Race-pregnancy group interactions P values: $P = .27$ for ΔHDL-C, $P = .37$ for ΔLDL-C, $P = .74$ for Δtotal cholesterol, and $P = .69$ for Δtriglycerides.

†Overall pregnancy group associations, P for: Pairwise comparisons corrected for multiple comparisons using the Dunnett's procedure; Group differences (primi- and multiparas) versus (nulligravidas): *$P < .05$, **$P < .01$, ***$P < .001$.

for white adolescents possibly because of the smaller sample of parous adolescents. Implications of our findings are that a more atherogenic lipid profile at younger ages could influence the long-term risk of cardiometabolic diseases in adulthood,[12] and fetal programming in future pregnancies.[29] Lower HDL-C levels associated with primiparity represent a 6% to 12% greater risk of CVD during midlife.[30] Greater parity also has been directly associated with greater risk of CVD in older women, although residual confounding remains an issue.[3,31]

Black–white differences in physical maturation and the overall pattern of adolescent growth are well known.[22,32] Black females reach menarche earlier, and have greater peak velocities in growth, followed slower growth in late adolescence than white females.[22] Pregnant adolescents tend to accrue more subcutaneous fat in central locations compared with adult women,[33,34] particularly younger, growing pregnant adolescents.[18] Previously, we reported that paras compared to nulligravid NGHS adolescents had greater increases in both BMI and waist circumference.[20] However, weight gain did not explain the lower HDL-C or greater triglycerides among paras in our analysis. The specific mechanism for the lipid changes is unclear, but insulin resistance does not explain our findings because the lower HDL-C and greater TG remained after controlling for change in BMI. Moreover, parity is not associated with increased incidence of type 2 diabetes after pregnancy in longitudinal studies,[35,36] except among women with a history of gestational diabetes mellitus (GDM),[36] which is uncommon in females <20 years of age.

Limitations include fewer white than black parous adolescents, variable ages for deliveries, later maturation of white girls, and the tendency for black adolescents to become pregnant at younger ages. We also did not have sufficient numbers of multiparas to assess whether decrements in HDL-C showed a threshold effect or a monotonic trend with higher order births. We adjusted for age at menarche, baseline lipid measurements, and sociodemographic covariates to minimize these differences, but they may still be influential. Hormonal contraceptive use during follow-up was a consequence of prior pregnancies, and appeared to mediate rather than confound our findings. Although we did not assess blood glucose and insulin in our models, adjustment for baseline BMI and changes in BMI during the 10-year period accounted for these metabolic characteristics which may result from excess fat deposition. Adolescents may have under-reported pregnancies ending in miscarriage or abortions which would bias our findings toward the null hypothesis.

The study strengths include the large, community-based sample of black and white girls that provides an internal comparison group of never pregnant adolescents to evaluate the direct effects of pregnancy on adolescent blood lipid profiles independent of growth in stature, maturation (age at menarche), and secular trends. Blood lipid measurements were obtained prospectively via standard research methodology both before and after pregnancies.

Our findings are potentially important because adolescence has been identified as one of the "critical periods" of growth and development that set the stage for future adult chronic disease, including diabetes and cardiovascular diseases.[37] Excessive fat deposition during adolescence may lead to persistent obesity,[38] elevated insulin, atherogenic lipids, and greater blood pressure levels into young adulthood.[39] Relevant to our findings, HDL-C and triglycerides are important predictors of future cardiovascular disease and possibly, diabetes in adulthood.[40] Furthermore, in black women, earlier age at a first birth (<20 years) has been associated with increasing rates of coronary heart disease.[31,41] Our findings show that pregnancy at an early age results in lowering of HDL-C and raising of triglycerides that is not explained by pregnancy-related weight retention. Pregnancy during adolescence may have even greater adverse effects on women's future cardiometabolic health in mid-life.

Conclusions

Pregnancy during adolescence or adulthood exerts lasting proatherogenic effects on blood lipids independent of weight gain. Future investigation is needed into the possible roles of lactation and central obesity as influencing the return of HDL-C and triglycerides to preconception levels, as well as prevention of long-term cardiometabolic diseases later in life. The demonstration of cardiovascular disease in early life gives credibility to risk factor examination of children and the need for beginning prevention and screening, particularly among parous adolescents.[37] Evaluation of lipid profiles among postpartum adolescents may identify those who would benefit from early lifestyle interventions, including adolescents who are not obese. Comprehensive behavioral interventions for postpartum adolescents could promote more favorable maternal blood lipids and glucose tolerance prior to conception, as well as newborn health in future pregnancies.[42]

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