Childhood Socioeconomic Circumstances, Inflammation, and Hemostasis Among Midlife Women: Study of Women's Health Across the Nation

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ABSTRACT

Background: Childhood socioeconomic status (SES) is related to risk for cardiovascular disease in adulthood, perhaps, in part, due to associations with inflammatory and hemostasis processes. We tested the hypotheses that childhood SES is related to C-reactive protein (CRP), fibrinogen, factor VIIc, and plasminogen activator inhibitor-1 (PAI-1) in midlife women and that the associations are mediated by adult SES and/or adult body mass index (BMI).

Methods: Using data from the prospective Study of Women's Health Across the Nation, we classified 1067 black and white women into 3 multidimensional childhood SES groups based on latent class analysis. Biological measures were assessed across 7 years along with covariates and mediators and analyzed by mixed regression models, followed by tests for mediation.

Results: Compared with women raised in high SES families, those from the lowest SES families had higher levels of CRP (b [standard error] = 0.37 [0.11]), PAI-1 (b = 0.23 [0.07]) factor VIIc (b = 0.05 [0.02]), and fibrinogen (b = 11.06 [4.89]), after adjustment for ethnicity, site, age, ratings of health between ages 11 and 18 years, visit, smoking status, menopausal status, stroke or heart attack, medications, and hormone use. Introduction of adult SES and BMI into the models reduced the childhood SES associations to nonsignificance for all four measures. Indirect mediation was apparent for adult education and BMI for CRP, and BMI for PAI-1.

Conclusions: Women raised in lower SES families had elevated markers of inflammation and hemostasis, in part, due to elevated BMI and education in adulthood.

Key words: Socioeconomic status, childhood, inflammation, hemostasis, race, women.

INTRODUCTION

Altered inflammation and hemostasis, two interrelated systems, play major roles in the pathophysiology of atherosclerosis and other vascular diseases. Hemostasis is the arrest of bleeding in response to injury. An abnormal response can lead to thrombosis or excessive bleeding, depending on the balance of multiple systems. Epidemiological studies have demonstrated the associations between biological measures of inflammation and hemostasis with risk for cardiovascular disease (CVD), with the evidence most substantial for C-reactive protein (CRP) and fibrinogen (1,2). CRP is a protein synthesized in the liver as an acute-phase reactant and is a nonspecific marker for inflammation, infection, and tissue damage (3). Fibrinogen is a glycoprotein synthesized in hepatocytes and is part of the platelet aggregation and coagulation process (4). There is less evidence of relations between other markers of

BMI = body mass index, **CRP** = C-reactive protein, **CVD** = cardiovascular disease, **CVs** = coefficients of variation, **PAI-1** = plasminogen activator inhibitor-1, **SES** = socioeconomic status, **SWAN** = Study of Women's Health Across the Nation

SDC Supplemental Content

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inflammation/hemostasis and CVD outcomes. Plasminogen-activator inhibitor type I (PAI-1) is synthesized in platelets and endothelial cells and serves as a major inhibitor of fibrinolysis, which should lead to an increase in arterial fibrin deposition and thrombosis (5). Factor VIIc is part of the coagulation cascade, but its role as a risk factor for CVD is controversial (6).

Accumulating data suggest that family socioeconomic status (SES) in childhood is related to risk for CVD (7), and understanding the mechanisms underlying these relations has been a topic of intense interest. A prominent hypothesis is that low childhood SES increases risk for inflammation and hemostasis, which, in turn, increases CVD risk. Large-scale studies have investigated the association of childhood SES and inflammation and hemostasis in adulthood. However, the results vary by measure of inflammation, measure of SES, demographic group, and covariates. Lower status parental occupation was related to higher CRP among adults in their 30s (8) and among the elderly (9). In the Atherosclerosis Risk in Communities Study, lower status parental occupation and education were related to higher fibrinogen levels and white blood cell count, particularly among whites (10). In other work, lower parental education was related to higher CRP levels among women but not among men (11). Brazilian men and women whose mothers had low education had elevated CRP (12). In a separate Brazilian sample, men whose families had higher income had elevated CRP and women whose mothers had low education had elevated CRP (13).

Investigators have questioned whether childhood SES is related to adult inflammation and hemostasis at least, in part, because low childhood SES leads to less education in adulthood, which leads to poor health behaviors in adulthood. Low childhood SES may be related to the development of obesity, which, in turn, may lead to a less favorable inflammatory and hemostasis profile (9). Few studies find that childhood SES has its effects on inflammation/hemostasis, independent of adult SES (e.g., (11)) but others report nonsignificant results, after adjusting for adult SES (12–14). Some studies consider body mass index (BMI) as one of a group of cardiovascular risk factors, so it is difficult to infer the specific mediational role of BMI in these models (10,14,15). One study controlled for birth weight and childhood BMI but not adult BMI, with the association remaining between childhood SES and adult CRP levels greater than 3 mg/dl (8).

Based on data from the Study of Women's Health Across the Nation (SWAN), the present report examines whether childhood SES is associated with four measures of inflammation and hemostasis: CRP, fibrinogen, factor VIIc, and PAI-1. Rather than examine individual aspects of family SES in childhood, women were classified into groups identified by latent class analysis using parental education and family assets. The latent class approach has advantages because it improves reliability and combines indices of status and resources, the major conceptual dimensions of SES, into one index. In addition to offering a combined childhood index of SES, the present study adds to the literature in a number of ways. This study includes a comprehensive set of inflammatory and hemostasis measures and examines the associations prospectively across a 7-year period when the biological measures were repeatedly assessed. It explores whether the associations vary by race or ethnicity. Finally, it tests the influence of several mediators: adult SES and BMI in adulthood. It is important to study women in particular because they have higher levels of inflammation than do men in midlife, there are unique determinants of inflammation in women, for example, use of hormone therapy (16–18), and the need to enhance understanding of cardiovascular risk in women in the perimenopausal and postmenopausal years.

METHODS

Sample

SWAN is a multisite, community-based, prospective study of aging and the menopause transition. From a cross-sectional study of 16,065 women from seven locations (Boston, Chicago, the Detroit area, Los Angeles, New Jersey, Oakland, and Pittsburgh), 3302 women who at the 1996 baseline were aged 42 to 52 years, had menstruated in the past 3 months, had an intact uterus and at least one ovary, were not using oral contraceptives or hormone therapy, and self-identified with designated race-ethnic groups were recruited for the prospective study. Details on sampling and recruitment methods are published elsewhere (19). Annual study visits between baseline and follow-up Year 13 included interviews; weight, height, and waist circumference; questionnaires; and a blood draw. The analytical sample for the present study includes participants from the four SWAN locations (Boston, Chicago, Detroit, and Pittsburgh) that administered the Childhood Context Ancillary Study questionnaire during visit 13. These sites enrolled black and white women. Among the 1399 SWAN participants across these sites, 1109 returned the ancillary questionnaire (response rate = 79%). From these participants, 30 were excluded due to having had a history of stroke or heart attack at baseline. Among the remaining women, we had inflammation and hemostasis data and relevant covariates for 1067 women. SWAN protocols were approved by the institutional review boards at each site, and each participant provided written informed consent.

Inflammation and Hemostasis Measures

Phlebotomy was performed in the morning after an overnight fast. Blood was maintained up to 1 hour at 4°C until separated and then frozen and sent on dry ice to the Medical Research Laboratory (Lexington, KY) for analysis. For budgetary reasons, assays were completed at baseline and at SWAN study years 1 and 3-7 for high-sensitivity CRP (hsCRP) and PAI-1, and at baseline and SWAN years 1, 3, 5, and 7 for factor VIIc and fibrinogen. All assays were measured in plasma. The hsCRP was quantitated using an ultrasensitive rate immunonephelemetric method (Dade-Berhing, Marburg, Germany). The sensitivity of the assay was .03 mg/dl and the coefficients of variation (CVs) at the concentrations of 0.05 and 2.2 mg/dl were 10% to 12%, and 5% to 7%, respectively. Fibrinogen and factor VIIc were measured in frozen citrated plasma (MLA ELECTRA 1400C; Medical Laboratory Automation Inc, Mt Vernon, NY) using a turbidometric detection system. Fibrinogen monthly interassay CVs were 2.3% to 3.5% and 2.6% to 3.6% at mean concentrations of 250 and 140 mg/dl, respectively,

and factor VIIc monthly interassay CVs were 7.8%, 5%, and 4% for mean activities of 8%, 45%, and 99% respectively. PAI-1 was measured with a sandwich procedure using a solid-phased monoclonal antibody and enzyme-labeled goat second antiserum for detection (IMUBIND plasma PAI-1 enzyme-linked immunosorbent assay; American Diagnostica, Greenwich, CT). PAI-1 monthly interassay CVs were 5% to 9% and 4% to 9% at mean concentrations of 7 and 22.5 ng/dl, respectively. Consistent with published guidelines, hsCRP values greater than 10 were excluded (11.8% of observations). All values except for fibrinogen were skewed and subjected to log transformation.

Childhood Circumstances

Information on childhood circumstances was collected with the 10-item Childhood Context Ancillary Study questionnaire that was administered during visit 13 in 2012/2013. To assess childhood SES, it asked participants about their mother's and father's highest educational level in six categories (e.g., less than high school and postgraduate degree). They were asked whether their family owned a car (yes/no) or home (yes/no) when they were children or teenagers. They were also asked whether their childhood family ever received public assistance (yes/no) and ever had difficulty paying for food or rent or making ends meet (yes/no) separately when they were younger than 11 or 11 to 18 years. These were combined into yes in either period versus no in all periods to be comparable in time frame to the other questions. In addition to the socioeconomic information, the questionnaire asked participants about their overall health when they were younger than 11 years and between 11 and 18 years old in five categories (excellent, very good, good, fair and poor). Participants were grouped into women reporting their childhood health as fair or poor health, very good or good, or excellent health at ages 11 to 18 years. All questions, with the exception of perceived child health questions, had been administered at SWAN Year 7 to 259 women at the Pittsburgh site. The concordance of the individual questions from Year 7 to Year 13 varied from 86.1% to 96.9% among these participants.

Adult Mediators and Covariates

We included race/ethnicity (black versus white), site, baseline age, and perceived health at ages 11 to 18 years as time-invariant covariates. Time varying covariates during the follow-up period were visit, current smoker (yes/no), menopausal status (postmenopausal, i.e., natural or surgical; late perimenopause, early perimenopause; premenopause; unknown, i.e., missing data or use of hormone therapy prevented accurate assessment of final menstrual period), heart attack or stroke, use of medications affecting inflammation and hemostasis (yes/no), and use of hormone therapy (yes/no). As potential mediators of the effects of childhood SES class, we included two indicators of adult SES measured at baseline, adult educational status (high school degree or less, some college, 4-year college degree or more) and financial hardship (very, somewhat, or not hard to pay for basics), and BMI (time varying).

Statistical Analysis

We identified distinctive subgroups of SWAN participants based on their childhood SES information using latent class analyses following recommended procedures in Mplus (20,21).

We used mixed-model linear regression using childhood SES class groups and covariates (time invariant: ethnicity, site, baseline age, ratings of health between ages of 11 and 18 years, and time varying: visit, smoking status, menopausal status, stroke or heart attack, medications, and hormone use) to predict each outcome separately across the 7 years of follow-up (Model 1). The predictor variable was childhood SES group, with highest SES group as the referent. p Values less than .05 for childhood SES group were considered statistically significant.

Using the same covariates in Model 1, analyses evaluated the association between childhood SES group and BMI at the same visits of the outcome measures, that is, 0, 1, and 3 to 7. Then we conducted two additional models: one including two indicators of SES, adult education and adult financial hardship (Model 2), and another adding adult education, financial hardship, and BMI (Model 3).

Mediational analyses varied for adult education and BMI. Because adult education was a categorical variable, ordinal logistic regression was used to test the relation between childhood SES latent class and adult education, as the dependent variable. Then the association between SES and outcome (e.g., logged CRP) while adjusting for adult education and other covariates was assessed by linear regression. Because the coefficients from ordinal logistic regression and linear regression had different scales, the coefficients were standardized (i.e., coefficient/standard error) so that they could be used in the analysis. Then the transformed coefficients were multiplied together to obtain the indirect effect (22). The indirect effects for BMI were obtained using linear regression as BMI was a continuous variable, with the effects of these variables estimated by the product of coefficients method (23). Confidence intervals of the indirect effects were estimated by bootstrap method with 1000 replications (24). We also tested for interactions between childhood SES classes and adult education groups, but none was statistically significant. All models were estimated with SAS version 9.3.

RESULTS

Sample Characteristics

Approximately 56% of the sample was white and 44% black (Table 1, left column), and 21% had a high school degree or less and 44% had a 4-year college degree or more (Table 2, left column). The number of smokers was small, and on average, the sample was overweight to obese.

Latent class analyses revealed that the women could be classified into three childhood SES groups. Class 1 contained 25 of the women and is the lowest SES, consisting of women with low-educated and poor parents, for example, family on public assistance (Table 1). Class 2 contained 51% of women with low-educated but nonpoor parents. Class 3 contained 24% of the women and is the highest SES, with high-educated and nonpoor parents. The analyses identified the three-class model as having the best fit. It had the lowest Bayesian Information Criterion score ($BIC_{1\text{-class}}$ = 12,112, $BIC_{2\text{-class}}$ = 11,545, $BIC_{3\text{-class}}$ = 11,453, $BIC_{4\text{-class}}$ = 11,473). In addition, the Vuong-Lo-Mendell-Rubin likelihood ratio test indicated that two classes are significantly better than one class ($p < .001$), three classes are better than two classes ($p = .076$), and four classes make no further improvement ($p = .816$). The three-class model also provides good classification quality. It has an entropy score of 0.712 (0.80 is considered high, 0.60 medium, and 0.40 low (25)). In addition, the correct class assignment probabilities are .86 for the lowest SES group, .85 for the middle SES group, and .93 for the highest SES group, which exceed the .70 recommended threshold (26). Because the entropy score was less than 0.80, we focused below on effects that were significant at $p < .01$, but report findings that are significant at $p < .05$.

The three childhood SES groups varied at baseline on smoking status, BMI, and initial menopausal status

TABLE 1. Distribution of Demographics and Childhood Socioeconomic Indicators Among Overall Sample and Within Three Latent Classes of Childhood Socioeconomic Conditions

		Distribution Within Latent Class		
Indicators	Full Sample	1 ("Adverse") Parents Low Educated and Poor	2 ("Fair") Parents Low Educated, Not Poor	3 ("Good") Parents High Educated, Not Poor
n	1067	271	539	257
Latent class membership, % columns sum to 100	—	25.4	50.5	24.1
Father's education, %				
Less than high school	28.3	35.1	37.1	2.7
High school credential	28.4	22.9	43.0	3.5
Technical or vocational school	5.1	1.5	9.1	0.4
Some college	10.5	7.4	9.3	16.3
Bachelor's degree	11.1	4.1	0.0	41.6
Postgraduate degree	8.7	2.2	0.0	33.9
Don't know	8.0	26.9	1.5	1.6
Mother's education, %				
Less than high school	26.5	40.6	30.8	2.7
High school credential	39.0	33.6	51.2	19.1
Technical or vocational school	7.1	4.4	8.4	7.4
Some college	11.3	5.5	8.7	22.6
Bachelor's degree	7.7	2.2	0.6	28.4
Postgraduate degree	4.8	1.1	0.0	18.7
Don't know	3.7	12.6	0.4	1.2
Childhood family, %				
...did not own a car	13.1	39.9	4.9	2.0
...did not own a home	20.1	63.1	6.2	4.3
...ever received public assistance	18.3	62.1	4.8	0.8
...ever had difficulty paying for food or rent	35.4	82.8	21.4	15.2
Race, %				
White	55.8	31.7	57.7	77.0
Black	44.2	68.3	42.3	23.0
SWAN location, %				
Boston	26.1	25.8	21.0	37.0
Chicago	14.3	13.7	13.5	16.3
Detroit	31.8	39.1	35.3	16.7
Pittsburgh	27.9	21.4	30.2	30.0

SWAN = Study of Women's Health Across the Nation

(Table 2). Women in the lower childhood SES group were more likely to be smokers and have higher BMI. Women in the lowest and highest childhood SES groups tended to be early perimenopausal compared with those in the middle group.

Women varied by childhood SES class in their levels of CRP, fibrinogen, and PAI-1 at baseline (Table 2). The values for CRP and fibrinogen increased monotonically with decreasing childhood SES ($p \leq .0001$ from linear trend analyses). Baseline factor VIIc was not related to childhood SES groups. The covariation of the individual indices that comprise the childhood latent classes with the measures of inflammation, hemostasis, and adult covariates is also presented in Table S1, Supplemental Digital Content 1, http://links.lww.com/PSYMED/A265.

All hemostasis and inflammatory measures were correlated. At baseline, CRP was associated with factor VIIc ($r = 0.26$), fibrinogen ($r = 0.59$), and PAI-1 ($r = 0.40$); factor

TABLE 2. Inflammation and Hemostasis Characteristics and Covariates at Baseline in the full Sample and According to Three Latent Classes of Childhood Socioeconomic Status (n = 1067)

Characteristics	Total Sample	Classes			p
		Low Parental Education, Poor	Low Parental Education, Not Poor	High Parental Education, Not Poor	
Baseline					
CRP, median (IQR), mg/l	1.6 (0.6–3.9)	2.1 (0.8–4.6)	1.7 (0.6–4.0)	1.1 (0.5–2.9)	<.0001
Fibrinogen, M (SD), mg/dl	301.5 (67.3)	312.4 (66.3)	302.5 (67.7)	287.6 (66.5)	<.0001
Factor VIIc %, median (IQR)	115.0 (98.0–132.0)	117.0 (98.0–136.0)	114.0 (98.0–132.0)	113.0 (96.0–128.0)	.60
PAI-1, median (IQR), ng/ml	21.1 (12.3–35.4)	23.4 (15.6–37.2)	19.7 (12.0–34.5)	20.4 (10.4–33.5)	.001
Smoker, yes, n (%)	176 (16.7)	66 (24.6)	83 (15.6)	27 (10.6)	<.0001
Body mass index, M (SD), kg/m^2	29.8 (7.7)	32.0 (8.6)	29.7 (7.3)	27.9 (6.8)	<.0001
Menopausal status, n (%)					.003
Premenopausal	570 (54.3)	123 (45.7)	298 (56.1)	149 (59.8)	
Early perimenopausal	479 (45.7)	146 (54.3)	233 (43.9)	100 (40.2)	
Adult education, n (%)					
High school or less	219 (20.8)	83 (31.0)	121 (22.7)	15 (5.9)	<.0001
Some college	371 (35.2)	109 (40.7)	204 (38.4)	58 (22.8)	
4-y college degree and higher	464 (44.0)	76 (28.4)	207 (38.9)	181 (71.3)	
Financial hardship, n (%)					<.0001
Hard	76 (7.1)	35 (12.9)	28 (5.2)	13 (5.1)	
Somewhat hard	293 (27.5)	93 (34.3)	154 (28.6)	46 (17.9)	
Not at all hard	698 (65.4)	143 (52.8)	357 (66.2)	198 (77.0)	

CRP = C-reactive protein; IQR = interquartile range; M = mean; SD = standard deviation.

p Values are unadjusted and are based on analysis of variance or χ^2.

VIIc was associated with fibrinogen (r = 0.12) and PAI-1 (r = 0.29), and fibrinogen was associated with PAI-1 (r = 0.19; all p values ≤ .0001).

Associations Between Childhood SES Class Groups and Inflammation, Hemostasis, and Adult Mediators

Independent of covariates, lower childhood SES was associated with higher CRP and PAI-1; the trends for fibrinogen and factor VIIc approached significance (Table 3, Model 1). The estimates for the low parental education/poor group differed significantly from high parental education/nonpoor group, but neither differed from the intermediate group (data not shown). Interactions with race and childhood SES class groups showed no significant relationships. Interactions of childhood SES class groups with visit number (0, 1, 3–7) showed no significant relationships for CRP or PAI-1, suggesting that the change over time in CRP or PAI-1 did not vary by childhood SES class groups.

Childhood SES groups varied in their education attainment reported at baseline (Table 2). Those in the low parental education/poor group were least likely to attain a college degree, whereas those in the high parental education/nonpoor group were most likely to attain a 4-year degree or higher. They also varied in reports of how hard it is to pay for basics, with those from families with low parental education/poor being most likely to report that it was hard.

Independent of covariates included in Model 1, neither adult education groups nor adult financial hardship was related to fibrinogen (p = .77 and p = .17) or to PAI-1 (p = .25 and p = .48), respectively. Adult education groups were related to CRP (p = .04) and factor VIIc (p = .04). Adult financial hardship was unrelated to CRP in the same model with education (p = .10) and tended to be related to factor VIIc (p = .06). Compared with women with a college degree, women with a high school degree or less tended to have higher CRP levels (estimate = 0.19 [standard error {SE} = 0.10], p = .06), and women with some college had higher CRP levels (estimate = 0.20 [SE = 0.09], p = .02) and factor VIIc levels (estimate = 0.04 [0.02], p = .01).

Independent of covariates included in Model 1, childhood SES class groups varied in BMI at years 0, 1, and 3-7, the visits concurrent with the biological measurement (p = .001). Compared with the highest childhood SES

TABLE 3. Estimates From Multiple Regression Mixed Models of Childhood Socioeconomic Status Predicting Inflammation and Hemostasis (n = 1067)

	Model 1		Model 2		Model 3	
Outcome Group Compared to Referent	*b* (SE)	*p*	*b* (SE)	*p*	*b* (SE)	*p*
C-reactive protein		.001		.03		.31
Low parental education, not poor	0.27 (0.09)	.002	0.19 (0.09)	.04	0.11 (0.07)	.13
Low parental education, poor	0.37 (0.11)	.001	0.27 (0.11)	.01	0.09 (0.09)	.34
Fibrinogen		.08		.23		.84
Low parental education, not poor	5.24 (4.08)	.20	3.38 (4.19)	.42	1.22 (3.77)	.75
Low parental education, poor	11.06 (4.89)	.03	8.54 (5.07)	.09	2.66 (4.58)	.56
Factor VIIc		.07		.27		.60
Low parental education, not poor	0.02 (0.02)	.15	0.01 (0.02)	.44	0.007 (0.02)	.68
Low parental education, poor	0.05 (0.02)	.02	0.03 (0.02)	.11	0.02 (0.02)	.33
PAI-1		.002		.02		.18
Low parental education, not poor	0.14 (0.06)	.01	0.12 (0.06)	.04	0.08 (0.05)	.11
Low parental education, poor	0.23 (0.07)	.001	0.20 (0.07)	.005	0.11 (0.06)	.09

SE = standard error; PAI-1 = plasminogen activator inhibitor-1.

Model 1: ethnicity, site, ratings of health at ages 11 to 18 years, baseline age, visit, smoking, menopausal status, heart attack or stroke, medications affecting outcomes, hormone use. Model 2: Model 1 + adult education and adult financial hardship. Model 3: Model 2 + body mass index.

p Values listed next to outcome reflect overall differences among the three class groups; *p* values listed next to class group compare the specific group to the referent group, high parental education and not poor.

group, women in the lowest childhood SES group had higher adult BMI over time (estimate = 2.13 [SE = 0.67], p = .002), as did women in the middle childhood SES group (estimate = 1.09 [SE = 0.56], p = .05).

Influence of Adult Education and BMI on the Associations Between Childhood SES Class Groups and Biological Measurements (Models 2 and 3)

Adjustments for adult education and financial hardship attenuated the relationships of childhood SES, with associations nonsignificant for factor VIIc and fibrinogen (Table 3, Model 2). Financial hardship was not related significantly to any of the outcomes in Model 2. Further adjustments for BMI reduced the relationship of childhood SES group and CRP and PAI-1 to nonsignificance (Table 3, Model 3). BMI was a highly significant predictor of all measures of inflammation and hemostasis (all p values < .0001 in Model 3; data not shown).

Mediational tests showed that indirect effects of adult education groups with adult financial hardship and BMI in the model were significant for CRP (14.74 [95% confidence interval {CI} = 2.76–28.30]) and nonsignificant for PAI-1. The indirect effects of adult BMI were significant for CRP (0.09 [95% CI = 0.02–0.16]) and for PAI-1 (0.05 [95% CI = 0.02–0.09]), with adult education groups and financial hardship in models. Mediational analyses were repeated with BMI from the immediately prior visit as a covariate on CRP and PAI-1 at visits 1 and 3–7. The indirect effects for prior BMI were also significant for CRP (0.07 [95% CI = 0.01–0.13]) and for PAI-1 (0.04 [95% CI = 0.004-0.07]).

Comparison of *b* values for childhood SES class showed that for CRP, they were reduced by 23% with adult education (treated as a pseudo-continuous variable) and by an additional 69% with BMI. The childhood SES class estimate for PAI-1 was reduced from Model 2 to Model 3 by 45% with BMI.

DISCUSSION

The present analysis showed that midlife women classified into one of three groups based on parental education and family assets varied in inflammation and hemostasis, with the women whose parents had little education and few assets having the highest levels. Adjustments were made for ethnicity, site, baseline age, perceived health at ages 11 to 18 years, visit, smoking, menopausal status, reports of heart attack or stroke, medications affecting outcomes, and hormone use. There was no evidence that the relationships varied by racial/ethnic status. Thus, childhood SES group was a strong predictor of measures of inflammation and hemostasis in midlife women.

We addressed statistically whether obtained associations might be due to women from lower childhood SES families achieving less education in adulthood and/or whether these women were more likely to have a higher BMI by adulthood. Our analyses suggested that childhood social class group was strongly related to adult education, which partially

mediated the associations with CRP. Further adjustment by adult BMI concurrent with measures of CRP and PAI-1 reduced the effects of childhood SES class to nonsignificance and accounted for a substantial portion of the childhood social class group estimates. Thus, these findings suggest that exposure to early childhood SES leads to both low educational attainment and risk for obesity in adult women, which, in turn, leads to elevated inflammation and hemostasis.

Our study had a number of limitations. Our childhood SES measures were retrospectively reported and collapsed across developmental stages. However, prior studies report that retrospective measures of childhood SES are reliable and accurate (27,28). In our own sample at one site, assessments of childhood SES 5 years apart were remarkably consistent. Our findings should not be extrapolated to other ages or to men. Because we did not measure childhood weight and height, we could not detect when prior to midlife the association of BMI and inflammation and hemostasis would begin to emerge. Note, however, that we did statistically control for the women's ratings of their health at ages 11 to 18 years, which is a more general indicator of health, albeit retrospective. Although we included a number of covariates in the model, some potentially significant covariates were not included, for example, asthma and physical activity.

We also did not have the data to access when in the life span prior to midlife associations of childhood SES and inflammation and hemostasis would emerge. An enumerative review concluded that the association between childhood SES and CRP in childhood and adolescence was inconsistent, with two positive studies of seven (29). This suggests that the associations may emerge in young adulthood or later. Earlier associations may also be apparent with more adverse childhood experiences. For example, one of the four SWAN sites had collected information regarding exposure to childhood abuse and neglect and found that independent of adult education, a history of child abuse was related to elevated CRP levels, in part, through adult obesity (30). Similarly, in the Dunedin Study, maltreatment in childhood prospectively measured was related to high CRP levels in young adult men and women (31). Several reviews of the literature suggest that exposure to interpersonal violence is related to the development of obesity, with associations being somewhat stronger in women than in men (32,33). Future research is needed to examine the types, intensity, and timing of adverse childhood experiences in relation to development of abnormal levels of inflammation and hemostasis in adulthood.

Our study has a number of strengths. We used repeated measures that reflect both hemostasis and inflammatory processes. We followed the women for 7 years and had extensive assessments of relevant covariates. Our analyses were able to show indirect effects of obesity and adult education in understanding the relationship of childhood SES and inflammation.

In summary, we found that black and white women who were raised in poor, less educated families had elevated levels of hemostasis and inflammation in adulthood. The associations for childhood SES were, in part, mediated by adult education and BMI. Prevention of obesity in low SES households may be one important strategy to reduce the negative consequences of low childhood SES on risk for CVD in adult women.

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