Research Article

JOURNAL OF CIRCULATING BIOMARKERS

Journal of Circulating Biomarkers
Volume 7: 1–10

DOI: 10.1177/1849454418779310
journals.sagepub.com/home/cbx
SAGE

Associations between smoking and lipid/lipoprotein concentrations among US adults aged ≥20 years

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Abstract

Cross-sectional data from National Health and Nutrition Examination Survey for the years 1999–2012 for those aged ≥20 years, fasting for at least 8 h, and classified as smokers and nonsmokers on the basis of observed serum cotinine levels were used to evaluate the impact of smoking on the adjusted and unadjusted concentrations of low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, total cholesterol (TC), and triglycerides (TG). Adjustments were made for the effects of gender; race/ethnicity; survey year; dietary intake of alcohol; caffeine; cholesterol; saturated, unsaturated, and total fatty acids; fasting time; body mass index; and poverty income ratio. Adjusted levels of LDL and TC did not vary among smokers and nonsmokers. Smokers had lower adjusted levels of HDL than nonsmokers (48.8 vs. 51.4 mg/dL, $p < 0.01$) and higher adjusted levels of TG (124.4 vs. 111.9 mg/dL, $p < 0.01$) than nonsmokers. Adjusted odds of smokers having abnormal levels were 1.6 (95% confidence interval (CI) 1.4–1.8) for HDL, 1.2 (95% CI 1.1–1.4) for TC, and 1.3 (95% CI 1.2–1.5) for TG. Males had lower adjusted levels than females for HDL (45.2 vs. 55.4 mg/dL, $p < 0.01$) and TC (191.3 vs. 196.6 mg/dL, $p < 0.01$) but higher adjusted levels than females for TG (126.3 vs. 110.1 mg/dL, $p < 0.01$) and LDL (114.4 vs. 112.6 mg/dL, $p = 0.02$). A unit increase in body mass index was associated with 1.4% decrease in the adjusted levels of HDL, 0.18% increase in the adjusted levels of LDL, and a 2.3% increase in the adjusted levels of TG.

Keywords

Smoking, triglyceride, cholesterol, lipids, lipoproteins, cotinine

Date received: 15 January 2018; accepted: 27 April 2018

Introduction

Smoking has been shown to alter lipid/lipoprotein levels. Komiya et al.[1] reported smokers with Brinkman index ≥ 554 (defined as the number of cigarettes smoked per day multiplied by duration of smoking in years) to have 1.657 times the odds of having abnormal triglyceride (TG) levels among Japanese males aged 24–68 years. Kuzuya et al.[2] also reported smokers to have lower levels of high-density lipoprotein (HDL), lower levels of low-density lipoprotein (LDL), lower levels of total cholesterol (TC), and higher levels of TG than nonsmokers. Based on a review of 54 published studies, when compared with nonsmokers, smokers were found to have higher levels of TC by 3%, TG levels by 9.1%, VLDL levels by 10%, LDL levels by 1.7%, and lower levels of HDL by 5.7%.[3] Furthermore, clear dose response relationships have been reported for TC, TG, and LDL findings.[4–6]

The presence of obesity, diabetes, and metabolic syndrome is of obvious importance to the studies of lipids. Among Japanese males aged 42–81 years, those who had visceral area ≥100 cm^2, also had higher proportion of abnormal TG (≥150 mg/dL), and this risk factor was

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further modified in relationship to their smoking status, with 18.8%, 17.3%, and 36.4% among nonsmokers, former smokers, and current smokers, respectively, but TG levels were not found to differ among these groups when visceral area was <100 cm^2.[7] Thus, an interaction between smoking and body fat distribution was found to affect TG levels. Håglin et al.[8] reported female smokers who never had type 2 diabetes and male smokers who currently had type 2 diabetes to have higher levels of TG than nonsmokers. The presence of the number of metabolic syndrome components was not reported to be affected by smoking.[9] Age may also be important, as De Souza et al.[10] reported an association between increased TG levels and smoking among elderly people aged ≥60 years.

A possible mechanism of how cigarette smoking may alter lipid levels in serum has been suggested.[6] Absorption of nicotine leads to secretion of catecholamines, cortisol, and growth hormones, activating adenyl cyclase in adipose tissue. This results in lipolysis of stored TG and release of free fatty acids. This, in turn, results in increased hepatic synthesis of TG and VLDL.

Recently, Jain[11] reported data from National Health and Nutrition Examination Survey (NHANES, https://www.cdc.gov/nchs/nhanes/index.htm) for the period 1999–2012 to investigate the effect of smoking on the levels of HDL, LDL, TC, and TG for US population aged ≥20 years, based upon self-reported use of tobacco products during the last 5 days to determine the smoking status of participants. However, Jain[12] reported on the possibility of bias in smoking classification based on self-reports. Using a cutoff of 10 ng/mL for serum cotinine to distinguish smokers from nonsmokers, 7.5% self-reported nonsmokers were found to be smokers and 2% self-reported smokers were found to be nonsmokers. In addition, for participants with missing self-reported smoking data, 20.8% were found to be smokers. Thus, there is a possibility that measured associations between smoking and lipid/lipoprotein levels may differ depending upon how smoking is classified. The current study was undertaken to evaluate associations between smoking and lipid/lipoprotein levels when smoking classification is based on the observed levels of serum cotinine, instead of self-reports. The hypothesis is that self-report introduces bias, and that cotinine measures will improve the evaluation. Smoking status will be determined by observed serum cotinine levels.

In addition to evaluation of lipid profile differentials among smokers and nonsmokers, based on serum cotinine levels, an extended objective of this study compares odds of having abnormal values (as defined in the next section) of HDL, LDL, TC, and TG among smokers when compared with nonsmokers. This has potential implications for surveillance and treatment of lipid abnormalities in smokers. Data from NHANES 1999–2012 were selected because NHANES provides data for a nationally representative sample of the non-institutionalized US population.

Methods

Data source and description

Data were obtained from NHANES (http://www.cdc.gov/nchs/nhanes/index.htm) for the years 1999–2012 for those ≥20 years old who have fasted for at least 8 h prior to blood draw. Data on demographics, body measures, physical activity, serum cotinine, total nutrient intake, HDL, LDL, TC, and TG levels were downloaded and match merged.

In NHANES, sampling weights are created for each sampling domain. Each sampling domain represents a specific combination of race/ethnicity, gender, age, and income. For NHANES survey 2011–2014, there were 87 sampling domains.[13] Examples of age groups for NHANES sampling domains included 1–2 years, 3–5 years, 6–11 years, . . . , 50–59 years, and ≥60 years. Each person within a sampling domain is assigned the domain weight whose value is based on sampling rate, response rate, and estimated US population for that sampling domain. For the purpose of analysis, sampling weight assigned to each person is taken into consideration. In addition, all analyses completed for this study used age as a continuous variable.

Sample sizes

Unweighted sample size for those aged ≥20 years and who have fasted for at least 8 h prior to blood draw was 15,267. Of the 15,267 participants for whom data were available, self-reported smoking status was unknown for 1031 participants while smoking status based on serum cotinine (<10 ng/ml classified as nonsmokers, ≥10 ng/mL classified as smokers) levels were unknown for 196 participants. Of the 3497 self-reported smokers, 281 or 8% were classified to be nonsmokers by the serum cotinine based status. Of 10,739 self-reported nonsmokers, 215 or 2% were classified as smokers based upon serum cotinine status. It was determined that there was enough discrepancy between self-reported and cotinine-based smoking status to possibly lead to discrepancy between the estimated unadjusted geometric means (UGM) and adjusted geometric means (AGM). In addition, a measured versus reported result decreases the percent of those with unknown smoking, thus providing a larger sample size. Weighted and unweighted sample sizes for non-missing values of HDL, LDL, TC, and TG by gender, race/ethnicity, and smoking status are given in Table 1. For some of the analyses conducted, the sample sizes were somewhat smaller because of missing values for physical activity levels and other variables.

Detailed age groupings among nonsmokers were as follows: $N_{\text{age: 20–29 years}} = 1891$, $N_{\text{age: 30–39 years}} = 1868$, $N_{\text{age: 40–49 years}} = 1805$, $N_{\text{age: 50–59 years}} = 1595$, $N_{\text{age: 60–69 years}} = 1907$, $N_{\text{age: 70–79 years}} = 1425$, and $N_{\text{age: ≥80 years}} = 938$. Detailed age groupings among smokers were as follows: $N_{\text{age: 20–29 years}} = 760$, $N_{\text{age: 30–39 years}} = 710$, $N_{\text{age: 40–49 years}} = 792$, $N_{\text{age: 50–59 years}} = 579$, $N_{\text{age: 60–69 years}} = 481$, $N_{\text{age: 70–79 years}} = 238$, and $N_{\text{age: ≥80 years}} = 82$.

Table 1. Unweighted and weighted sample sizes by gender, race/ethnicity, and smoking status for non-missing values of HDL, LDL, TC, and TG for NHANES 1999–2012.

		N	Weighted *N*	%
HDL	Total	15,092	1,441,274,994	100.0
	Male	7261	693,906,283	48.1
	Female	7831	747,368,711	51.9
	Non-Hispanic White	7245	1,009,503,646	70.0
	Non-Hispanic Black	2859	158,639,515	11.0
	Mexican American	2953	113,347,185	7.9
	Other race/ethnicities	2035	159,784,649	11.1
	Nonsmoker	11,401	1,057,412,610	73.7
	Smoker	3626	377,377,356	26.3
LDL	Total	14,717	1,406,279,496	100.0
	Male	7003	668,584,457	47.5
	Female	7714	737,695,039	52.5
	Non-Hispanic White	7053	983,805,516	70.0
	Non-Hispanic Black	2824	156,746,995	11.1
	Mexican American	2846	109,670,666	7.8
	Other race/ethnicities	1994	156,056,319	11.1
	Nonsmoker	11,140	1,034,353,625	73.9
	Smoker	3514	365,674,864	26.1
TC	Total	15,091	1,441,201,566	100.0
	Male	7261	693,906,283	48.1
	Female	7830	747,295,283	51.9
	Non-Hispanic White	7245	1,009,503,646	70.0
	Non-Hispanic Black	2858	158,566,086	11.0
	Mexican American	2953	113,347,185	7.9
	Other race/ethnicities	2035	159,784,649	11.1
	Nonsmoker	11,400	1,057,339,182	73.7
	Smoker	3626	377,377,356	26.3
TG	Total	15,073	1,439,979,380	100.0
	Male	7250	693,096,765	48.1
	Female	7823	746,882,615	51.9
	Non-Hispanic White	7241	1,008,921,734	70.1
	Non-Hispanic Black	2850	158,238,706	11.0
	Mexican American	2948	113,067,635	7.9
	Other race/ethnicities	2034	159,751,305	11.1
	Nonsmoker	11,388	1,056,627,236	73.7
	Smoker	3620	376,867,116	26.3

HDL: high-density lipoprotein; LDL: low-density lipoprotein, TC: total cholesterol; TG: triglyceride; NHANES: National Health and Nutrition Examination Survey.

Derived variables

Self-reported levels of recreational physical activity were categorized as vigorous, moderate, none, or minimal. For the NHANES years 2007–2012, activity status was enquired during a typical week and during the last 30 days for NHANES 1999–2006. Those who self-reported being engaged in vigorous activity with or without being engaged in moderate activity were classified as being engaged in vigorous activity. Those who self-reported being engaged in moderate activity without being engaged in vigorous activity were classified as being engaged in moderate activity. Those who did not answer the question about their recreational physical activity were considered to be engaged in minimal or no physical activity.

Abnormal values of HDL and TG were defined consistent with Wildman et al.[14]: abnormal fasting triglyceride levels were $\geq$150 mg/dL; abnormal HDL levels were <40 mg/dL for males or <50 mg/dL for females. While variable risk-based abnormal values for LDL and TC have been suggested (https://www.nhlbi.nih.gov/files/docs/guidelines/atp3xsum.pdf), for the purpose of this communication, LDL values were considered to be abnormal LDL $\geq$ 130 mg/dL. TC values were considered to be abnormal for TC $\geq$ 240 mg/dL.

Software

SAS University Edition software (www.sas.com) was used to analyze data for this study.

Statistical analyses

UGMs with 95% confidence intervals for HDL, LDL, TC, and TG levels by gender, race/ethnicity, and smoking status were computed by SAS Proc SURVEYREG. UGMs by gender, race/ethnicity, and smoking status are given in Table 2.

For the adjusted analysis, log 10-transformed values of HDL, LDL, TC, and TG were used as dependent variables in regression analyses done by SAS Proc SURVEYREG. Categorical independent variables used in regression models were gender (males and females), race/ethnicity (non-Hispanic White (NHW), non-Hispanic Black (NHB), Mexican Americans (MA), and other unclassified race/ethnicities (OTH)), smoking status (nonsmoker and smoker), and physical activity level (vigorous, moderate, none, or minimal). Continuous independent variables used in regression models were age, age^2, body mass index, fasting time in hours, poverty income ratio (PIR), total daily dietary intake of total cholesterol, alcohol, caffeine, carbohydrate, fiber, monounsaturated fatty acids, polyunsaturated fatty acids, saturated fatty acids, total fat, and survey year. However, because of very high correlations between monounsaturated fatty acids, polyunsaturated fatty acids, saturated fatty acids, and total fat may have led to multicollinearity, one variable at a time was entered in the model, and as such, there were four fitted models for each dependent variable. AGMs with 95% confidence intervals are given in Table 3. Table 4 provides data on associations (slopes) of continuous variables such as PIR with HDL, LDL, TC, and TG. In order to compute adjusted odds of having abnormal levels of HDL, LDL, TC, and TG, SAS Proc SURVEYLOGISTIC was used with abnormal values (yes, no) of lipids/lipoproteins as dependent variables and independent variables, similar to the linear regression mentioned above except that dietary variables were not used. While the objectives of this study intended to evaluate the impact of smoking on the adjusted and unadjusted levels of LDL, HDL, TC, and TG as well as the adjusted odds of having abnormal levels of LDL, HDL, TC, and TG among smokers, the adjusted analyses did make

Table 2. Unadjusted geometric means with 95% confidence intervals for HDL, LDL, TC, and TG by gender, race/ethnicity, and smoking status for those aged ≥20 years.

	HDL	LDL	TC	TG
Total	51.1 (50.7–51.5)	112.4 (111.6–113.2)	193.8 (192.8–194.8)	115.5 (113.8–117.2)
M	46.1 (45.7–46.5)	113.2 (112.1–114.2)	191.2 (189.9–192.5)	124.2 (121.6–126.8)
F	56.2 (55.6–56.7)	111.8 (110.7–112.8)	196.3 (195–197.5)	108 (106–109.9)
NHW	51.1 (50.6–51.6)	113.1 (112.1–114.1)	195.2 (193.9–196.5)	118.6 (116.6–120.7)
NHB	53.8 (53.2–54.5)	109.3 (108–110.7)	187.8 (186.4–189.2)	90 (87.6–92.6)
MA	48.3 (47.7–48.9)	112 (110.3–113.7)	192 (190.1–193.9)	125.2 (121.2–129.2)
OTH	50 (49–51)	111.7 (109.5–113.9)	192.4 (190.1–194.7)	117.8 (113.8–121.9)
NSM	52.1 (51.7–52.5)	112.4 (111.5–113.3)	194.1 (193–195.2)	113.2 (111.3–115.2)
SM	48.3 (47.7–49)	112.2 (110.8–113.7)	192.7 (191–194.4)	121.8 (119.1–124.6)
Statistically significant differences	M < F ($p < 0.01$), NHW < NHB ($p < 0.01$), NHW > MA ($p < 0.01$), NHB > MA ($p < 0.01$), NHB > OTH ($p < 0.01$), NSM > SM ($p < 0.01$)	NHW > NHB ($p < 0.01$), NHB < MA ($p = 0.02$)	M < F ($p < 0.01$), NHW > NHB ($p < 0.01$), NHW > OTH ($p = 0.01$), NHW < OTH ($p = 0.04$), NHB < MA ($p < 0.01$), NHB < OTH ($p < 0.01$)	M > F ($p < 0.01$), NHW > NHB ($p < 0.01$), NHW < MA ($p < 0.01$), NHB < MA ($p < 0.01$), NHB < OTH ($p < 0.01$), MA > OTH ($p = 0.01$), NSM < SM ($p < 0.01$)

Source: Data from National Health and Nutrition Examination Survey 1999–2012.
HDL: high-density lipoprotein; LDL: low-density lipoprotein, TC: total cholesterol; TG: triglyceride; M: male; F: female; NHW: non-Hispanic White; NHB: non-Hispanic black; MA: Mexican American; OTH: other race/ethnicities; NSM: nonsmoker; SM: smoker.

Table 3. Adjusted geometric means with 95% confidence interval for fasting levels of HDL, LDL, TC, and TG in mg/dL for participants aged ≥20 years by gender, race/ethnicity, smoking, and physical activity status.

		HDL	LDL	TC	TG
Gender	M	45.2 (42.3–48.3)	114.4 (107.7–121.5)	191.3 (183–200)	126.3 (111.4–143.3)
	F	55.4 (51.9–59.2)	112.6 (105.9–119.7)	196.6 (188.2–205.3)	110.1 (97.5–124.5)
Race/ethnicity	NHW	49.2 (45.9–52.6)	114.4 (107.5–121.7)	195.5 (186.9–204.5)	125.5 (111–141.8)
	NHB	54.2 (50.7–57.9)	111 (104.5–118)	189.3 (181.4–197.7)	89.8 (79.3–101.7)
	Mexican American (MA)	48.5 (45.4–51.8)	115.1 (108.1–122.5)	196.7 (188.1–205.6)	134.2 (118.3–152.2)
	OTH	48.6 (45.4–52.1)	113.5 (106.6–120.7)	194.3 (185.7–203.2)	128.1 (112.4–146)
Smoking	NSM	51.4 (48.1–54.9)	113.6 (106.9–120.7)	193.9 (185.5–202.7)	111.9 (98.9–126.6)
	SM	48.8 (45.6–52.1)	113.3 (106.6–120.4)	193.9 (185.6–202.6)	124.4 (109.7–141)
Physical activity	VIG	50.4 (47.1–53.9)	115.5 (108.4–123)	195.2 (186.6–204.1)	114.6 (101.5–129.5)
	MOD	49.2 (45.9–52.6)	114.5 (107.5–121.9)	194.4 (185.7–203.5)	120.4 (105.6–137.3)
	MIN	50.7 (47.4–54.1)	110.5 (104.2–117.2)	192.2 (184.2–200.6)	119 (105.1–134.6)
Statistically significant differences		M < F ($p < 0.01$), NHW < NHB ($p < 0.01$), NHB > MA ($p < 0.01$), NHB > OTH ($p < 0.01$), NSM > SM ($p < 0.01$), VIG < MOD ($p < 0.01$), MOD < MIN ($p = 0.01$)	M > F ($p = 0.02$), NHW > NHB ($p < 0.01$), NHB < MA ($p < 0.01$), VIG > MIN ($p = 0.02$), MOD > MIN ($p < 0.01$)	M < F ($p < 0.01$), NHW > NHB ($p < 0.01$), NHB < MA ($p < 0.01$), NHB < OTH ($p = 0.01$)	M > F ($p < 0.01$), NHW > NHB ($p < 0.01$), NHW < MA ($p < 0.01$), NHB < MA ($p < 0.01$), NHB < OTH ($p = 0.01$), NSM < SM ($p < 0.01$), VIG < MOD ($p < 0.01$)

Source: Data from National Health and Nutrition Examination Survey 1999–2012.
HDL: high-density lipoprotein; LDL: low-density lipoprotein, TC: total cholesterol; TG: triglyceride; M: male; F: female; NHW: non-Hispanic White; NHB: non-Hispanic black; MA: Mexican American; OTH: other race/ethnicities; NSM: nonsmoker; SM: smoker; VIG: vigorous; MOD: moderate; MIN: none or minimal.

adjustments for the simultaneous and interacting effects of age, gender, race/ethnicity, and other variables. This statistical adjustment mechanism resulted in impact of age, gender, race/ethnicity, and other variables also being evaluated on the adjusted levels of LDL, HDL, TC, and TG as well as the odds of having abnormal levels of LDL, HDL, TC, and TG.

Results

Univariate analysis

Unadjusted geometric means. Males had lower UGMs than females for HDL (46.1 vs. 56.2 mg/dL, $p < 0.01$, Table 2) and TC (191.2 vs. 196.3 mg/dL, $p < 0.01$, Table 2) but higher UGMs than females for TG (124.2 vs. 108.0 mg/

Table 4. Regression slopes with significance probabilities for independent variables when log10-transformed values of HDL, LDL, TC, and TG in mg/dL were fitted as dependent variables.[a]

	Dependent variables as Log 10 of			
Independent variables	HDL	LDL	TC	TG
Age	0.00051 (0.19)	**0.00937 (<0.01)**	**0.0072 (<0.01)**	**0.00913 (<0.01)**
Age^2	0 (0.81)	**−0.00009 (<0.01)**	**−0.00006 (<0.01)**	**−0.00007 (<0.01)**
Body mass index	**−0.0059 (<0.01)**	**0.00078 (<0.01)**	0.0001 (0.49)	**0.01006 (<0.01)**
PIR	**0.00591 (<0.01)**	**−0.00287 (0.01)**	**−0.00147 (0.03)**	**−0.00878 (<0.01)**
Survey year	**0.00611 (<0.01)**	**−0.008 (<0.01)**	**−0.00436 (<0.01)**	**−0.01032 (<0.01)**
Fasting time (h)	0.00075 (0.19)	0.00167 (0.03)	**0.00117 (0.01)**	0.00018 (0.89)
Alcohol intake (g)	**0.00059 (<0.01)**	−0.00009 (0.11)	**0.00015 (<0.01)**	0.00008 (0.44)
Caffeine intake (mg)	0 (0.6)	**0.00002 (<0.01)**	0 (0.42)	**−0.00005 (<0.01)**
Cholesterol intake (mg)	0 (0.53)	0.00001 (0.38)	0 (0.37)	0.00001 (0.63)
Dietary fiber (g)	**0.00091 (<0.01)**	−0.00033 (0.07)	−0.00009 (0.4)	**−0.00142 (<0.01)**
Total fat (g)	**0.00022 (<0.01)**	0.00001 (0.81)	0.00002 (0.55)	**−0.00044 (<0.01)**
Monounsaturated fatty acids (g)	**0.00043 (<0.01)**	0 (0.97)	0.00003 (0.72)	**−0.0009 (<0.01)**
Polyunsaturated fatty acids (g)	**0.00063 (<0.01)**	−0.00025 (0.08)	**−0.00022 (0.03)**	**−0.00175 (<0.01)**
Saturated fatty acids (g)	**0.0005 (0.01)**	0.00024 (0.06)	**0.00022 (0.01)**	**−0.00059 (0.01)**
R^2 in %	27.8	6.1	8.9	17.2

Source: Data from National Health and Nutrition Examination Survey 1999–2012.
HDL: high-density lipoprotein; LDL: low-density lipoprotein, TC: total cholesterol; TG: triglyceride; PIR: poverty income ratio.
[a]Statistically significant slopes are shown in bold letters.

dL, $p < 0.01$, Table 2). Among the three major race/ethnic categories, UGMs for HDL were NHB (53.8 mg/dL) > NHW (51.1 mg/dL) > MA (48.3 mg/dL), and all three pairwise differences were statistically significant ($p < 0.01$, Table 2). UGMs for LDL were NHW > NHB (113.1 vs. 109.3 mg/dL, $p < 0.01$) and NHB < MA (109.3 vs. 112.0 mg/dL, $p = 0.02$, Table 2). UGMs for TC were NHW (195.2 mg/dL) > MA (192.0 mg/dL) > NHB (187.8 mg/dL), and all three pairwise differences were statistically significant ($p < 0.01$, Table 2). UGMs for TG were MA (125.2 mg/dL) > NHW (118.6 mg/dL) > NHB (90.0 mg/dL), and all three pairwise differences were statistically significant ($p < 0.01$, Table 2). Smokers had lower UGMs than nonsmokers for HDL (48.3 vs. 52.1 mg/L, $p < 0.01$) but higher UGMs than nonsmokers for TG (121.8 vs. 113.2 mg/L, $p < 0.01$). Jain[11] also found smokers to have lower UGMs for HDL than nonsmokers (48.2 vs. 52.1 mg/dL, $p < 0.01$) but higher TG than nonsmokers (123.2 vs. 113.5 mg/dL, $p < 0.01$). UGMs among smokers and nonsmokers were not found to differ for LDL and TC for the study conducted by Jain.[11]

Multivariate analysis

Adjusted geometric means. Males had lower AGMs than females for HDL (45.2 vs. 55.4 mg/dL, $p < 0.01$, Table 3) and TC (191.3 vs. 196.6 mg/dL, $p < 0.01$, Table 3) but higher AGMs than females for TG (126.3 vs. 110.1 mg/dL, $p < 0.01$, Table 3) and LDL (114.4 vs. 112.6 mg/dL, $p = 0.02$, Table 3). Among three major race/ethnic categories for HDL, AGMs were in the following order: NHB (54.2 mg/dL) > NHW (49.2 mg/dL) > MA (48.5 mg/dL) and NHW > NHB ($p < 0.01$) and NHB > MA ($p < 0.01$). AGMs for LDL were NHW > NHB (114.4 vs. 111.0 mg/dL, $p < 0.01$) and NHB < MA (111.0 vs. 115.1 mg/dL, $p < 0.01$). AGMs for TC were NHW > NHB (195.5 vs. 189.3 mg/dL, $p < 0.01$) and NHB < MA (189.3 vs. 196.7 mg/dL, $p < 0.01$). Among three major race/ethnic categories for TG, AGMs were in the following order: MA (134.2 mg/dL) > NHW (125.5 mg/dL) > NHB (89.8 mg/dL), and all three pairwise differences were statistically significant ($p < 0.01$). As expected, nonsmokers had higher HDL AGMs than smokers (51.4 vs. 48.8 mg/L, $p < 0.01$) and lower AGMs for TG (111.9 vs. 124.4 mg/L, $p < 0.01$) than nonsmokers. Contrary to this, Jain[11] found smokers to have higher HDL (52.2 vs. 50.1 mg/dL, $p = 0.02$) than nonsmokers using self-reported data. Vigorous physical activity was associated with higher HDL than moderate physical activity (50.4 vs. 49.2 mg/dL, $p < 0.01$, Table 3), but other than this, there were no clear dose-response relationships for exercise and outcomes with the exception of a paradoxical relationship for LDL for which vigorous and moderate physical activity were associated with higher LDL (115.5 and 114.5 vs. 110.5 mg/dL, $p \leq 0.02$, Table 3) than none or minimal physical activity.

Associations between dependent and continuous independent variables. As expected, positive association ($p < 0.01$, Table 4) was found between age and LDL ($\beta = 0.00937$), TC ($\beta = 0.0072$), and TG ($\beta = 0.00913$) but age^2 had a negative association ($p < 0.01$, Table 4) with the adjusted levels of LDL ($\beta = -0.00009$), TC ($\beta = -0.00006$), and TG ($\beta = -0.00007$). The increase in adjusted levels of LDL, TC, and TG with age is therefore shown to attenuate as people age. Depending upon the relative slopes associated with age and age^2, the direction of change in LDL, TC, and

Table 5. Percent prevalence with 95% confidence intervals for abnormal values of HDL (<40 mg/dL for males, <50 mg/dL for females), LDL (>130 mg/dL), TC (>240 mg/dL), and TG (>150 mg/dL).

	HDL	LDL	TC	TG
Total	29.6 (28.5–30.8)	34 (32.9–35.1)	14.6 (13.8–15.3)	29.5 (28.4–30.6)
M	27.1 (25.6–28.6)	35 (33.6–36.5)	13.1 (12.1–14.1)	33.4 (31.8–35)
F	32 (30.5–33.5)	33.1 (31.7–34.4)	16 (15–16.9)	25.9 (24.6–27.2)
NHW	29.5 (27.9–31)	34.5 (33.1–35.9)	15.5 (14.5–16.5)	31.1 (29.8–32.3)
NHB	24.2 (22.2–26.2)	31.8 (29.9–33.7)	11.5 (10.3–12.6)	15.3 (13.7–16.9)
MA	35.1 (32.7–37.4)	34.3 (32.1–36.6)	12.7 (11.3–14)	34.3 (31.9–36.6)
OTH	32.2 (28.8–35.6)	32.6 (29.8–35.4)	13 (11.3–14.8)	30.3 (27.4–33.2)
NSM	27.4 (26.3–28.5)	33.7 (32.5–34.9)	14.2 (13.4–15.1)	28.5 (27.3–29.8)
SM	35.7 (33.4–38)	34.5 (32.8–36.3)	15.3 (14–16.7)	32.2 (30.4–34)
Statistically significant differences	M < F ($p < 0.01$), NHW > NHB ($p < 0.01$), NHW < MA ($p < 0.01$), NHB < MA ($p < 0.01$), NHB < OTH ($p < 0.01$), NSM < SM ($p < 0.01$)	M > F ($p = 0.04$), NHW > NHB ($p < 0.01$), NHB < MA ($p = 0.03$)	M < F ($p < 0.01$), NHW > NHB ($p < 0.01$), NHW > MA ($p < 0.01$), NHW < OTH ($p = 0.02$)	M > F ($p < 0.01$), NHW < NHB ($p < 0.01$), NHW < MA ($p = 0.02$), NHB < MA ($p < 0.01$), NHB < OTH ($p < 0.01$), MA > OTH ($p = 0.04$), NSM < SM ($p < 0.01$)

Source: Data from National Health and Nutrition Examination Survey 1999–2012.
HDL: high-density lipoprotein; LDL: low-density lipoprotein, TC: total cholesterol; TG: triglyceride; M: male; F: female; NHW: non-Hispanic White; NHB: non-Hispanic black; MA: Mexican American; OTH: other race/ethnicities; NSM: nonsmoker; SM: smoker.

TG may reverse at a specific age. As expected, BMI was negatively associated ($\beta = -0.0059$, $p < 0.01$) with the levels of HDL but positively associated ($p < 0.01$) with the levels of LDL ($\beta = 0.00078$) and TG ($\beta = 0.0106$). A measure of income above poverty level (PIR) was positively associated ($\beta = 0.00591$, $p < 0.01$) with the levels of HDL and negatively associated ($p \leq 0.03$) with the levels of LDL ($\beta = -0.00287$), TC ($\beta = -0.00147$), and TG ($\beta = -0.00878$). This is an expected finding.

Alcohol intake was positively associated ($p < 0.01$) with HDL ($\beta = 0.00059$) and TC ($\beta = 0.00015$). Caffeine intake was positively associated with LDL ($\beta = 0.00002$, $p < 0.01$, Table 4) but negatively associated with TG ($\beta = -0.00005$, $p < 0.01$). Intakes of dietary fiber ($\beta = 0.00091$), total fat ($\beta = 0.00022$), monounsaturated fatty acids ($\beta = 0.00043$), polyunsaturated fatty acids ($\beta = 0.00063$), and saturated fatty acids ($\beta = 0.0005$) were positively associated with the levels of HDL ($p \leq 0.01$). Intakes of dietary fiber ($\beta = -0.00142$), total fat ($\beta = -0.00044$), monounsaturated fatty acids ($\beta = -0.0009$), polyunsaturated fatty acids ($\beta = -0.00175$), and saturated fatty acids ($\beta = -0.00059$) were negatively associated with the levels of TG ($p \leq 0.01$). Intake of polyunsaturated fatty acids ($\beta = -0.00022$, $p = 0.03$) was negatively associated with TC and dietary intake of saturated fatty acids ($\beta = 0.00022$, $p = 0.01$, Table 4) was positively associated with TC.

Prevalence and odds of having abnormal levels

As compared to females, males had lower prevalence of abnormal (low) levels of HDL (27.1% vs. 32%, $p < 0.01$, Table 5) and lower prevalence of abnormal (high) TC (13.1% vs. 16%, $p < 0.01$). It should be recalled that the defined low abnormal HDL is a higher value for females than for males, so the comparison can be confusing. Males had higher prevalence of the abnormal (high) levels of LDL (35.0% vs. 33.1%, $p = 0.04$, Table 5) and TG (33.4% vs. 25.9%, $p < 0.01$). The prevalence of abnormal levels of HDL by race/ethnicity was MA (35.1%) > NHW (29.2%) > NHB (24.2%), and all three pairwise differences were statistically significant ($p < 0.01$). The prevalence of abnormal levels of LDL by race/ethnicity was NHW (34.5%) > MA (34.3%) > NHB (31.8%) and NHW > NHB and NHB < MA ($p = 0.03$). For TC, the prevalence of the abnormal levels by race/ethnicity was NHW (15.5%) > MA (12.7%) and NHB (11.5%). The prevalence of abnormal levels of TG by race/ethnicity was MA (34.3%) > NHW (31.1%) > NHB (15.3%), and all three pairwise differences were statistically significant ($p \leq 0.02$, Table 5).

As compared to females, adjusted odds of males having abnormal levels of HDL was 0.737 (0.662–0.820, Table 6) and for abnormal levels of TC, it was 0.819 (0.785–0.914, Table 6). As compared to females, adjusted odds of males having abnormal levels of LDL was 1.113 (1.021–1.212, Table 6) and for abnormal levels of TG, it was 1.48 (1.335–1.639, Table 6). As compared to NHW, adjusted odds of abnormal levels of HDL, LDL, TC, and TG for NHB were 0.512, 0.871, 0.713, and 0.330, respectively (Table 6) and adjusted odds for MA were 1.109, 1.082, 0.940, and 1.282, respectively. Smokers had higher odds of having abnormal levels of HDL (1.596, 1.141–1.802) and TG (1.308, 1.155–1.481).

A 10-year change in age was associated with markedly higher odds of abnormal levels of LDL (3.585, 3.004–4.278), TC (4.12, 3.763–5.154), and TG (1.887, 1.553–2.92). For one unit change in BMI, odds of having abnormal levels of HDL, LDL, TC, and TG were 1.559, 1.061, 1.007, and 1.442. For a unit increase in PIR, odds of having abnormal levels of HDL was 0.888 (0.853–0.924) and for TG, it was 0.936 (0.906–0.968). For each survey period,

Table 6. Adjusted odds of having abnormal levels of HDL (<40 mg/dL for males, < 50 mg/dL for females), LDL (>130 mg/dL), TC (>240 mg/dL), and TG (>150 mg/dL) by gender, race/ethnicity, smoking status.[a]

Effect	HDL	LDL	TC	TG
Males versus Females	0.737 (0.662–0.82)	**1.113 (1.021–1.212)**	**0.819 (0.735–0.914)**	**1.48 (1.335–1.639)**
Non-Hispanic Blacks versus non-Hispanic Whites	0.512 (0.443–0.591)	**0.871 (0.768–0.988)**	**0.713 (0.616–0.825)**	**0.33 (0.285–0.382)**
Mexican Americans versus non-Hispanic Whites	1.109 (0.959–1.282)	**1.082 (0.957–1.223)**	**0.94 (0.798–1.107)**	**1.282 (1.131–1.453)**
Other race/ethnicities versus non-Hispanic Whites	1.098 (0.914–1.319)	**0.943 (0.81–1.099)**	**0.861 (0.721–1.028)**	**1.086 (0.913–1.291)**
Smoker versus non-Smoker	1.596 (1.414–1.802)	**1.073 (0.979–1.176)**	**1.228 (1.07–1.409)**	**1.308 (1.155–1.481)**
Vigorous versus none/minimum physical activity	1.065 (0.884–1.283)	**1.137 (0.928–1.394)**	**0.983 (0.745–1.296)**	**0.896 (0.756–1.061)**
Moderate versus none/minimum physical activity	1.287 (1.078–1.537)	**1.152 (0.99–1.341)**	**1.174 (0.919–1.5)**	**1.084 (0.916–1.283)**
Age for a 10-year change	0.914 (0.766–1.091)	**3.585 (3.004–4.278)**	**4.12 (3.235–5.246)**	**1.887 (1.553–2.292)**
Age^2 for a change of 100	1.001 (0.983–1.019)	**0.891 (0.876–0.907)**	**0.887 (0.868–0.907)**	**0.954 (0.937–0.972)**
Body mass index for a unit change	1.559 (1.491–1.63)	**1.061 (1.022–1.101)**	**1.007 (0.963–1.052)**	**1.442 (1.38–1.507)**
PIR for a unit change	0.888 (0.853–0.924)	**0.956 (0.922–0.991)**	**0.944 (0.905–0.984)**	**0.936 (0.906–0.968)**
Fasting for a 1-h change	0.992 (0.968–1.016)	**1.039 (1.014–1.064)**	**1.033 (1.002–1.065)**	**0.991 (0.966–1.017)**
Survey year for a 2-year change	0.879 (0.848–0.912)	**0.918 (0.886–0.951)**	**0.935 (0.889–0.984)**	**0.911 (0.879–0.945)**

Source: Data from National Health and Nutrition Examination Survey 1999–2012.
HDL: high-density lipoprotein; LDL: low-density lipoprotein, TC: total cholesterol; TG: triglyceride; PIR: poverty income ratio.
[a]Physical activity level, age, body mass index, PIR, and survey year. Statistically significant odds ratios are shown in bold letters.

odds of having abnormal levels of HDL, LDL, TC, and TG decreased by 0.879, 0.918, 0.935, and 0.911, respectively (Table 6).

Discussion

As previously mentioned, there are two ways to assess smoking status. Study participants may be asked to self-report their smoking status. But, at times, the accuracy of self-reports may be questionable. The accuracy of self-reports may depend on the specificity of the questions asked. In addition, there may be intentional misreporting. The respondents may report what they think is a socially acceptable smoking status. As discussed elsewhere,[12] in the current social setting, smokers are more likely to report themselves as nonsmokers than nonsmokers reporting themselves as smokers. Thus, if the accuracy of smoking status is needed, use of one or the other biomarkers of tobacco smoke becomes a desirable alternative. Proposed biomarkers of tobacco smoke include serum cotinine, urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL),[15] volatile organic compounds like benzene and toluene measured in blood,[16] and urinary thiocyanate.[17] However, probably because of the ease of measurement using easily available assays, serum cotinine continues to remain a biomarker of choice. The half-life of serum cotinine is estimated to be 16–19 h,[18] and as such, serum cotinine can only be used as a biomarker of exposure to tobacco smoke during the last 5 days. On the other hand, half-life of urinary NNAL has been estimated to be as much as 10–18 days,[19] and as such, urinary NNAL can be used as the exposure to tobacco smoke during the last 6–12 weeks.[19] These data might suggest urinary NNAL as a preferred biomarker of exposure to tobacco smoke. However, the assay used to measure NNAL is complicated and expensive and NHANES data for NNAL did not become available until NHANES 2007–2008. Since the study period for this communication was between 1999 and 2012, serum cotinine was selected as a biomarker of tobacco smoke.

Based on a study among 215 patients, Jarvis et al.[20] proposed a serum cotinine cut off of 14 ng/mL to distinguish smokers from nonsmokers. As far as we could determine, first mention of nonsmokers having <10 ng/mL of serum cotinine was also by Jarvis et al.[18] However, since serum cotinine reflects exposure to tobacco smoke from all sources including main stream and second hand smoke, Benowitz et al.[21] proposed a serum cotinine cut off of 2.99 ng/mL for adolescents aged 12–19 years and 3.08 ng/mL for adults aged $\geq$20 years to distinguish smokers from nonsmokers. These substantially lower cutoffs reflected reduction in exposure to secondhand smoke over 1988–2002 in US as documented by Pirkle et al.[22] However, Benowitz et al.[21] used self-reported smoking status as the Gold Standard to develop the proposed serum cotinine cutoffs as presented above. In other words, proposed cutoffs by Benowitz et al.[21] depended upon the accuracy of self-reported smoking status. The use of cutoffs that depended upon the accuracy of self-reported smoking status would have been contrary to the objectives of this study. As such, we used the serum cotinine cutoff of 10 ng/mL for this study.

Many, if not all, of the studies that have previously investigated the association between smoking and lipid/

lipoprotein levels were in specific communities, not necessarily for a representative sample of the entire national population under investigation. This nationally representative sample of the US population aged ≥20 years used cotinine-based classification to distinguish smokers from nonsmokers and, therefore, is different from both community-based studies and previous results reported by Jain.[11] The use of the biomarker reclassified about 10% of participants by smoking class and increased the sample size by 5.9%. Advantages of the biomarker cotinine have been reported extensively,[23] and the accuracy of adult self-report has also been reported.[24] Our findings support the inference that use of the biomarker is particularly pertinent for the analysis of prevalence data, such as found in NHANES.

Effect of smoking

NHANES data reveal that the levels of both HDL and TG are adversely affected among smokers, a finding that is in the literature but which could be further emphasized in risk factor and tobacco control literature. Compared to nonsmokers, adjusted levels among smokers were about 6% lower for HDL and 11% higher for TG, both undesirable associations. Prevalence of abnormal or low levels of HDL among smokers was 8.3% higher than nonsmokers. The prevalence of abnormal or elevated levels of TG was 3.7% higher among smokers than nonsmokers. Odds of having abnormal levels for smokers was about 60% higher for HDL and about 31% higher for TG than nonsmokers. In spite of the differences in study design and populations covered, some of the results of this study are consistent with the results reported by Komiya et al.,[1] Koda et al.,[7] Devaranavadgi et al.,[6] Meenakshisundaram et al.,[4] Craig et al.,[3] and Gossett et al.[5]

Effect of age, race/ethnicity, and gender

Consistent with the literature, increase in age was found to be associated with increases in the adjusted levels of LDL, TC, and TG. However, the associations are not monotonic and attenuate with increasing age. Despite the attenuation, a 10-year increase in age was associated with higher odds of abnormal levels of LDL (OR: 3.6), TC (OR: 4.1), and TG (OR: 1.9) as per definitions used in this study. Similar results using commercial clinical laboratory data have been reported by Kaufman et al.[25]

In a study conducted in Anniston, Alabama, United States, Aminov et al.[26] reported African Americans to have lower levels of total lipids and triglycerides and higher levels of HDL among those who were not on any lipid lowering medications. Santos et al.[27] compared results in a Brazilian population by race: Blacks were reported to have a favorable profile, higher concentrations of HDL but lower concentrations of LDL and TG. Similar to these findings, we report that NHB did have higher levels of HDL and lower levels of TC and TG (Table 3) and, in addition, as compared to NHW, NHB had lower odds (Table 6) of having abnormal values of HDL (OR: 0.512), LDL (OR: 0.871), TC (OR: 0.713), and TG (OR: 0.33).

In this study, males were found to have higher adjusted levels of LDL and TG than females and lower adjusted levels of HDL and TC than females (Table 3). Gender differences in lipid/lipoprotein metabolism have been reported by Russo et al.,[28] Habib et al.,[29] Kolovou et al.,[30] Duvernoy et al.,[31] Wang et al.,[32] and others. Males having higher levels of LDL than females have been reported by Kaufman et al.[25] and Russo et al.[28] Females having higher levels of HDL than males have been reported by Habib et al.,[29] Russo et al.,[28] Kolovou et al.,[30] and Duvernoy et al.[31] Lower levels of TG among females as compared to males have been reported by Habib et al.,[29] Russo et al.,[28] Kolovou et al.,[30] and Duvernoy et al.[31] Kolovou et al.[30] reported females to have higher levels of TC than males. As compared to females, males had lower odds (Table 6) of clinically "abnormal" HDL (OR: 0.737) and TC (0.819) but higher odds of abnormal LDL (OR: 1.113) and TG (OR: 1.48). The HDL comparison for abnormal values requires understanding of the different cut-offs used. Since we normally think of females as having favorable cardiovascular risk profiles until the age of menopause, the population data may provide additional detail to inform clinical risk factor considerations.

Conclusion

Results of this study do indicate that smoking is associated with adverse lipid/lipoprotein profiles among adult population of the United States. Smokers were shown to have lower adjusted levels of HDL and higher adjusted levels of TG, as well as higher adjusted odds of having abnormal levels of HDL, LDL, and TG when compared with nonsmokers.

Use of serum cotinine rather than self-reports improves understanding of the relationship between smoking and unfavorable lipid profile.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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