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Apolipoprotein B is More Strongly Associated with Cardiovascular Risk Factors than Low-Density Lipoprotein Cholesterol in Young-to-Middle Aged Adults

Aniqa Alam

ABSTRACT

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By

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Cardiovascular disease (CVD) is the leading cause of death in the United States. Medical practitioners and public health officials alike consider atherosclerosis, in which plaque buildup leads to the hardening of arteries, to be one of the main culprits in CVD morbidity and mortality. Measuring low-density lipoprotein cholesterol (LDL-C) has been touted as an effective proxy for assessing the risk for atherosclerosis. However, new emerging evidence show that traditional lipid biomarkers, such as LDL-C, may not be as robust in CVD prediction as previously thought. Apolipoproteins, which are involved in the creation of lipoproteins, have been shown to be effective predictors of CVD events, even more so than LDL-C in some cases, but previous research have also established a non-linear trend with apolipoprotein B (ApoB) distribution when age is involved. Therefore, in light of past research, this study aims to examine potential differential associations between ApoB, LDL-C, and cardiovascular risk factors in the context of age groups. Using the 2013-2014 cycle of the National Health and Nutrition Examination Survey, we observed Spearman correlations and Wilcoxon/Kruskal-Wallis scores between various CVD risk factors (e.g.: body mass index, hypertension, diabetes status, etc.) and ApoB and LDL-C across two age cohorts. We found that ApoB has a special relationship with the younger cohort that does not manifest with LDL-C, and that this relationship attenuates in the older cohort. Based off of these results along with previous studies, assessment of CVD risk among the young would benefit from including ApoB in the already established battery of biomarkers.

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APPROVAL PAGE

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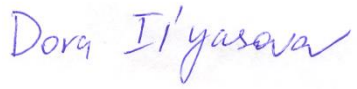

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Author's Statement Page

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Introduction

Cardiovascular disease (CVD) is the leading cause of death in the United States (Gu, Paulose-Ram, Burt, & Kit, 2014) and according to the American Heart Association one American will die of a coronary event every 1 minute and 23 seconds (Go et al., 2014). Medical practitioners and public health officials alike consider atherosclerosis, in which plaque buildup leads to the hardening of arteries, to be one of the main culprits in CVD morbidity and mortality (Singh, Mengi, Xu, Arneja, & Dhalla, 2002).

Measuring low-density lipoprotein cholesterol (LDL-C) has been touted as an effective proxy for assessing the risk for atherosclerosis. However, new emerging evidence show that traditional lipid biomarkers, such as LDL-C, may not be as robust in CVD prediction as previously thought (Chan & Watts, 2006). This lack of sensitivity in CVD prediction is especially concerning when considering that statins and other medications are often the first lines of defense in attempting to reduce the risk of atherosclerosis by targeting LDL-C (Riccioni and Sblendorio, 2012). From 2011 to 2012, nearly 28% percent of adults over the age of 40 admitted to using lipid-lowering medication (Gu, Paulose-Ram, Burt, & Kit, 2014). If LDL-C's sensitivity in predicting CVD events is not effective as previously believed, then focusing mainly on LDL-C may not be assessing the true risk of atherosclerosis and CVD. Nontraditional biomarkers need to be investigated in order to improve sensitivity in CVD prediction. One such class of nontraditional biomarkers to be considered are apolipoproteins.

Apolipoproteins are a family of proteins involved in the synthesis of lipoproteins, which transport lipids such as cholesterol and triglycerides through circulation (Feingold & Grunfeld, 2000). They are crucial to the formation of various forms of cholesterol-carrying lipoprotein particles, including LDL-C and high-density lipoprotein cholesterol (HDL-C). Apolipoprotein B (ApoB) in particular has been shown to be associated with atherosclerosis and atherosclerotic heart disease events and may be an even better predictor of CVD events than traditional LDL-C counts (Gigante et al., 2012; Lamarche et al., 1996). Many of our recommendations in the health care system concerned with reducing cardiovascular risk are based on our understanding that atherosclerotic risk is tied uniquely to LDL-C. In recent literature, however, ApoB has been increasingly shown to be associated with cardiovascular risk, even more so than LDL-C (Sniderman, Islam, Yusuf, & McQueen, 2013). ApoB has also been shown to be associated with carotid atherosclerosis (Steffen et al., 2017) and with coronary artery calcification in young adults (Wilkins, Li, Sniderman, Chan, & Lloyd-Jones, 2016).

Age is a major factor in the incidence of CVD events. Advanced age in particular has been proven to be significantly associated with heart disease (Castelli, 1984), but youth is not always protective in terms of cardiovascular risk. In fact, in a landmark study by Enos, Holmes, and Beyer (1951), autopsies performed on 300 United States soldiers killed during the Korean War showed subclinical atherosclerosis among those in their late teens and early adulthood. Subclinical atherosclerosis in the young with metabolic syndrome can often be a sign of premature heart disease (Tzou et al., 2005), and as global population trends sway more towards metabolic dysfunction (Go et al., 2014), it seems all the more pertinent to focus preventative interventions in young adulthood as well as retirement age.

Bachorik, Lovejoy, Carroll, and Johnson (1997) examined the third national health and nutrition examination survey (NHANES III) conducted between 1988 and 1991. They aimed to examine the distribution of apolipoprotein B and A1 among men and women in the United States and found that ApoB largely followed LDL-C distribution throughout age, but increasingly diverged in older age. Among men, Bachorik and colleagues (1997) found an overall trend of increasing median ApoB levels as age progressed, followed by a plateau in middle-age, ending with a decrease in old age. In women, this pattern was also evident, but was modified with two plateau periods: one in early adulthood and another in post-menopausal stage. Building off of these conclusions and other previous research, this study aims to examine potential differential associations between ApoB, LDL-C, and cardiovascular risk factors in the context of age groups.

Methods

To examine the relationship between ApoB and CVD risk factors versus LDL-C and CVD risk factors, we utilized NHANES from the 2013-2014 cycle. At the time of analysis, this was the most recent iteration of the survey available. NHANES employs a complex sampling strategy to represent the American population as a whole. However, for the purposes of this study, we did not require nationally representative data, and therefore, did not apply weights. Rather, the aim was to examine serum ApoB and LDL levels within the same individual, and explore the influence of age on the relationship between these biomarkers and CVD risk factors.

The total population of NHANES 2013-2014 consists of 10,175 individuals, with 6,261 being between the ages of 17 and 80 years. The study cohort was divided into two age groups: those aged 18-50 and 51-80. The cutoff point between the two age groups was chosen based off of the findings of Bachorik and colleagues (1997), in which they found menopause-induced hormone changes to be the

cause of the double plateau in women. Variables of interest included gender, race, body mass index (BMI), socioeconomic status, high-density lipoprotein cholesterol (HDL-C), triglycerides, diabetes status, blood pressure, and smoking status.

Serum ApoB, LDL-C, HDL-C, and triglyceride measurements were derived from venipuncture samples collected on mobile examination centers. Measurements for serum ApoB, LDL-C, and triglycerides are only available if participants were 12 years and above and were examined in the morning. HDL-C measurements were available for those aged 6 years and above. NHANES set a reported age cutoff as 80, with those above the age of 80 being entered into the system as "80". BMI was calculated as weight in kilograms divided by height in meters-squared. Data on income-to-poverty was available and used as a proxy for socioeconomic status, along with educational status. The income-to-poverty ratio (ItPR) was calculated by dividing household family income by the state-established poverty guidelines. Values were not reported if the reported income was less than or equal to $20,000, and the cutoff point was at a ratio of 5.00. Race was split into four levels: non-Hispanic black, non-Hispanic white, Mexican-American, and "Other". The category "Other" consists of all races not previously named, including Asian. For the purpose of analysis, diabetes status was coded dichotomously. Diabetes was confirmed if the participants reported "yes" to the question "Have you ever been told by a doctor or health professional that you diabetes or sugar diabetes?" and/or if they were found to have blood glycohemoglobin levels of 6.5% and above. Blood glycohemoglobin measurements were also collected from mobile examination centers. Smoking status was confirmed if participants answered "Yes" to at least one of the following questions: "Have you smoked at least 100 cigarettes in your entire life?", "Do you now smoke cigarettes?", "During the past 5 days, including today, did you smoke cigarettes, pipes, cigars, little cigars or cigarillos, water pipes, hookahs, or e-cigarettes?", and "During the past 5 days, including today, did you use any smokeless tobacco (i.e. chewing tobacco, snuff, snus, or dissolvables)?". NHANES measured systolic and diastolic blood pressure three times for each participant, with a fourth measurement being included if one of the past three attempts were incomplete. The readings were averaged across the three measurements to produce a single measurement for analysis. It was also used to detect the presence of hypertension, which was defined as systolic blood pressure of 130 mmHg and above and/or diastolic blood pressure of 85 mmHg and above.

For each age cohort, Spearman correlations were observed for serum ApoB and LDL-C levels with age (measured in years), BMI, HDL-C, triglycerides, and ItPR. Wilcoxon rank sum and Kruskal-Wallis scores were generated for ApoB and LDL-C levels by sex, race, educational status, diabetes status, smoking status, and presence of hypertension. All analyses were run on SAS 9.3.

Results

Table 1. Demographic Characteristics by Age Cohort [a] [b]

Characteristics	17-80 Cohort		17-50 Cohort		51-80 Cohort	
		N = 6261		*N = 3586*		*N = 2675*
Age (Years)	46 (31-62)	*N Missing (%) = 0*	33 (23-42)	*N Missing (%) = 0*	64 (58-73)	*N Missing (%) = 0*
		N = 5761		*N = 3304*		*N = 2457*
Income-to-Poverty Ratio	2.02 (1.02-3.93)	*N Missing (%) = 500 (7.99)*	1.84 (0.91-3.82)	*N Missing (%) = 282 (7.86)*	2.18 (1.12-4.13)	*N Missing (%) = 218 (8.15)*
Gender						
Male	2994 (47.82)		1716 (47.85)		1278 (47.78)	
Female	3267 (52.18)		1870 (52.15)		1397 (52.22)	
N		*6261*		*3586*		*2675*
N Missing (%)		*0*		*0*		*0*
Ethnicity						
Non-Hispanic White	2609 (41.67)		1359 (37.90)		1250 (46.73)	
Non-Hispanic Black	1292 (20.64)		723 (20.16)		569 (21.27)	
Mexican-American	879 (14.04)		570 (15.90)		309 (11.55)	
Other	1481 (23.65)		934 (26.05)		547 (20.45)	
N		*6261*		*3586*		*2675*
N Missing (%)		*0*		*0*		*0*
Education (Recode education)						
Less than 9th Grade	463 (7.40)		160 (4.47)		303 (11.34)	
9-11th Grade	1049 (16.77)		676 (18.87)		373 (13.96)	
High School Grad/GED	1449 (23.17)		822 (22.95)		627 (23.47)	
Some College/AA	1850 (29.58)		1108 (30.93)		742 (27.77)	
College Grad	1443 (23.07)		816 (22.78)		627 (23.47)	
N		*6254*		*3582*		*2672*
N Missing (%)		*7 (0.11)*		*4 (0.11)*		*3 (0.11)*

[a] Continuous variables: median (IQR)

[b] Categorical variables: frequencies (%)

Table 2. Lipid Profile by Age Cohort [a]

Characteristics	17-80 Cohort		17-50 Cohort		51-80 Cohort	
Apolipoprotein B	87 (71-104)	*N = 2759* *N Missing (%) = 3502 (55.93)*	84 (69-101)	*N = 1543* *N Missing (%) = 2043 (56.97)*	91 (75-106)	*N = 1216* *N Missing (%) = 1459 (54.54)*
Low-density Lipoprotein (LDL)	107 (84.5-131)	*N = 2720* *N Missing (%) = 3541 (56.56)*	104 (84-127)	*N = 1514* *N Missing (%) = 2072 (57.78)*	111 (86-135)	*N = 1206* *N Missing (%) = 1469 (54.92)*
High-density Lipoprotein (HDL)	50 (42-61)	*N = 5769* *N Missing (%) = 492 (7.86)*	49 (41-59)	*N = 3288* *N Missing (%) = 298 (8.31)*	51 (42-64)	*N = 2481* *N Missing (%) = 194 (7.25)*
Triglycerides	93 (63-141)	*N = 2760* *N Missing (%) = 3501 (55.92)*	86 (58-129)	*N = 1544* *N Missing (%) = 2042 (56.94)*	102 (70.5-150)	*N = 1216* *N Missing (%) = 1459 (54.54)*

[a] Continuous variables: median (IQR)

Table 3. Metabolic and Other Risk Factors by Age Cohort [a] [b]

Characteristics	17-80 Cohort		17-50 Cohort		51-80 Cohort	
		N = 5987		*N = 3434*		*N = 2553*
Body Mass Index (kg/m3)	27.6 (23.8-32.3)	*N Missing (%) = 274 (4.38)*	27.1 (23.2-32.0)	*N Missing (%) = 152 (4.24)*	28.1 (24.7-32.7)	*N Missing (%) = 122 (4.56)*
		N = 5852		*N = 3347*		*N = 2505*
Systolic (mmHg)	119 (109-132)	*N Missing (%) = 409 (6.53)*	115 (107-123)	*N Missing (%) = 239 (6.66)*	129 (117-141)	*N Missing (%) = 170 (6.36)*
		N = 5836		*N = 3344*		*N = 2492*
Diastolic (mmHg)	69 (62-77)	*N Missing (%) = 425 (6.79)*	69 (62-76)	*N Missing (%) = 242 (6.75)*	71 (62-77)	*N Missing (%) = 183 (6.84)*
High Blood Pressure						
Hypertension	1730 (29.56)		518 (15.48)		1212 (48.38)	
No Hypertension	4122 (70.44)		282 (84.52)		1293 (51.62)	
N		*5852*		*3347*		*2505*
N Missing (%)		*409 (6.53)*		*239 (6.66)*		*170 (6.36)*
Diabetes Status						
Diabetes	877 (14.01)		195 (5.44)		682 (25.50)	
No Diabetes	5384 (85.99)		3391 (94.56)		1993 (74.50)	
N		*6261*		*3586*		*2675*
N Missing (%)		*0*		*0*		*0*
Smoking Status						
Ever Smoked	2787 (44.58)		1428 (39.92		1359 (50.80)	
Never Smoked	3465 (55.42)		2149 (60.08)		1316 (49.20)	
N		*6252*		*3577*		*2675*
N Missing (%)		*9 (0.14)*		*9 (0.14)*		*0*

[a] Continuous variables: median (IQR)

[b] Categorical variables: frequencies (%)

Table 4. Associations Between ApoB/LDL-C and Demographic Characteristics [a b]

Characteristics	17-80 Cohort		17-50 Cohort		51-80 Cohort	
	ApoB	LDL-C	ApoB	LDL-C	ApoB	LDL-C
Age (Years)	.185 (<.0001)	.112 (<.0001)	.352 (<.0001)	.303 (<.0001)	-.187 (<.0001)	-.226 (<.0001)
Income-to-Poverty Ratio	.031 (.120)	.065 (.001)	.046 (.085)	.065 (0.015)	-.015 (.621)	.051 (.087)
Gender						
Male	88.0 (72.0-106.0)	106.0 (83.0-133.0)	87.0 (71.0-107.0)	107.0 (84.0-133.0)	89.0 (73.0-105.0)	105.0 (82.0-132.0)
Female	86.0 (71.0-102.0)	107.0 (86.0-130.0)	81.0 (67.0-97.0)	101.0 (83.0-122.0)	93.0 (76.0-107.0)	116.0 (92.0-138.0)
P-value	*0.019*	*0.546*	*<.0001*	*0.002*	*0.024*	*<.0001*
Ethnicity						
Non-Hispanic White	86.5 (72.0-103.0)	106.0 (84.0-130.0)	85.0 (70.0-103.0)	105.0 (84.0-130.0)	88.0 (73.0-104.0)	106.0 (83.0-131.0)
Non-Hispanic Black	81.0 (67.0-100.0)	104.0 (82.0-130.0)	77.0 (64.0-94.0)	99.0 (80.0-124.0)	88.0 (72.0-101.0)	110.0 (85.0-138.0)
Mexican-American	90.5 (75.0-109.0)	108.5 (89.0-129.5)	89.0 (73.0-108.0)	106.5 (87.0-129.0)	93.0 (80.0-111.0)	111.5 (91.0-130.0)
Other	90.0 (72.0-106.0)	110.0 (86.0-134.0)	85.0 (68.0-100.0)	103.0 (84.0-125.0)	99.0 (82.0-111.0)	121.0 (91.0-143.0)
P-value	*<.0001*	*0.116*	*<.0001*	*0.103*	*<.0001*	*0.001*
Education (Recode education)						
Less than 9th Grade	91.0 (75.0-109.0)	110.0 (87.0-134.0)	88.0 (73.0-109.0)	109.5 (89.0-131.0)	92.0 (76.0-111.0)	110.0 (86.0-134.0)
9-11th Grade	85.0 (71.0-102.0)	103.0 (81.0-128.0)	81.0 (68.0-99.0)	102.0 (80.0-121.0)	91.0 (75.0-104.0)	105.0 (83.5-135.0)
High School Grad/GED	87.0 (71.0-103.5)	108.0 (85.0-133.0)	85.0 (68.0-103.0)	105.5 (85.0-133.0)	90.0 (75.0-104.0)	110.0 (86.0-132.0)
Some College/AA	87.0 (71.0-104.0)	106.0 (85.0-129.0)	83.0 (69.0-102.0)	103.0 (84.0-126.0)	93.0 (74.0-106.0)	113.5 (87.0-134.0)
College Grad	87.0 (71.0-103.0)	107.0 (86.0-133.0)	85.0 (68.0-100.0)	104.0 (85.0-129.0)	89.5 (73.0-107.0)	112.0 (88.0-137.0)
P-value	*0.0624*	*0.15*	*0.598*	*0.216*	*0.666*	*0.724*

[a] Continuous variables: Spearman correlation (P-value)

[b] Categorical variables: Median (Interquartile Range)

Demography:

Age showed to be associated with both ApoB and LDL-C in all age cohorts. The younger cohort demonstrated a moderate positive association with age (ApoB: r = .352, p<.0001; LDL-C: r = .303, p<.0001) while ApoB and LDL-C showed to be negatively associated with age in the older cohort (ApoB: r = -.187, p<.0001; LDL-C: r = -.226, p<.0001). In all cases, ApoB had a stronger association with age than LDL-C, regardless of the direction of the association. ItPR had a significant, albeit weak, association with LDL-C (r = .065, p=.015) among the general and younger cohort. Otherwise, ItPR showed no association with ApoB nor with LDL-C in the older cohort.

ApoB was associated with gender in all age cohorts, while LDL-C was associated with gender in both age groups. It is worth noting that men had significantly higher median ApoB and LDL-C levels within the younger cohort. In the younger cohort, median ApoB and LDL-C (IQR) were 87.0 (71.0-107.0) and 107.0 (84.0-133.0) among males and 81.0 (67.0-97.0) and 101.0 (83.0-122.0) among females, respectively. However, this pattern is reversed in the older cohort, with women returning higher median

ApoB and LDL-C values (IQR) of 93.0 (76.0-107.0) and 116.0 (92.0-138.0), compared to men with median values (IQR) of 89.0 (73.0-105.0) and 105.0 (82.0-132.0), respectively. ApoB was associated with race in all age cohorts, whereas LDL-C was only associated with race in the older cohort. African Americans returned the lowest median ApoB values in the younger cohort, but there was less of a disparity among their senior counterparts. In the case of LDL-C in the older generation, the "other" race category had the highest median values out of all the levels of race. Elevated levels of ApoB were also prevalent in the older cohort, whereas Mexican-Americans held this distinction in the younger cohort. Education was not associated with ApoB nor LDL-C in any age category.

Table 5. Associations Between ApoB/LDL-C and Lipids [a]

Characteristics	17-80 Cohort		17-50 Cohort		51-80 Cohort	
	ApoB	LDL-C	ApoB	LDL-C	ApoB	LDL-C
High-density Lipoprotein (mg/dL)	-.224 (<.0001)	-.020 (.307)	-.284 (<.0001)	-.109 (<.0001)	-.181 (<.0001)	.066 (.021)
Triglycerides (mg/dL)	.526 (<.0001)	.252 (<.0001)	.570 (<.0001)	.325 (<.0001)	.438 (<.0001)	.144 (<.0001)

[a] Continuous variables: Spearman correlation (P-value)

Lipids:

ApoB was negatively associated with HDL-C in all age cohorts. LDL-C was negatively associated with HDL-C in the younger cohort ($r = -.109$, $p<.0001$), while the older cohort showed a weak positive association ($r = .066$, $p=.021$). In all instances, ApoB presented a stronger association than LDL-C with HDL-C. Triglycerides were associated with both ApoB and LDL-C in every age category. Once again, ApoB had a far stronger correlation with triglycerides than LDL-C in all cohorts.

Table 6. Associations Between ApoB/LDL-C and Metabolic and Other Risk Factors [a] [b]

Characteristics	17-80 Cohort		17-50 Cohort		51-80 Cohort	
	ApoB	LDL-C	ApoB	LDL-C	ApoB	LDL-C
Body Mass Index (kg/m²	.229 (<.0001)	.128 (<.0001)	.332 (<.0001)	.246 (<.0001)	.056 (.054)	-.039 (.176)
Diabetes Status						
Diabetes	88.0 (72.0-105.0)	98.0 (75.0-122.0)	93.0 (76.0-120.0)	101.0 (82.0-125.0)	86.5 (71.0-101.0)	96.5 (73.5-120.0)
No Diabetes	87.0 (71.0-103.0)	108.0 (87.0-132.0)	83.0 (68.0-100.0)	104.0 (84.0-127.0)	92.0 (76.0-107.0)	115.0 (91.0-138.0
P-value	*0.152*	*<.0001*	*0.0001*	*0.857*	*0.003*	*<.0001*
Smoking Status						
Ever Smoked	88.0 (72.0-106.0)	105.0 (83.0-132.0)	87.0 (71.0-105.0)	105.0 (84.0-130.0)	90.0 (72.0-106.0)	106.0 (82.0-133.0
Never Smoked	86.0 (71.0-102.0)	107.0 (86.0-130.0)	81.0 (68.0-100.0)	103.0 (83.0-125.0)	92.0 (77.0-106.0)	115.0 (90.0-137.0
P-value	*0.036*	*0.545*	*0.0007*	*0.139*	*0.122*	*0.003*
Blood Pressure						
Systolic (mmHg)	.172 (<.0001)	.107 (<.0001)	.201 (<.0001)	.132 (<.0001)	.051 (.078)	.032 (.280)
Diastolic (mmHg)	.201 (<.0001)	.167 (<.0001)	.249 (<.0001)	.187 (<.0001)	.132 (<.0001)	.136 (<.0001)
High Blood Pressure						
Hypertension	92.0 (74.0-109.0)	109.0 (87.0-136.0)	91.0 (72.0-111.0)	109.0 (87.0-136.0)	92.0 (74.5-107.0)	109.0 (87.0-136.0
No Hypertension	85.0 (70.0-102.0)	105.0 (83.0-129.0)	82.0 (68.0-99.0)	103.0 (83.0-125.0)	90.0 (75.0-105.0)	113.0 (85.5-134.0
P-value	*<.0001*	*0.001*	*<.0001*	*0.006*	*0.2572*	*0.592*

[a] Continuous variables: Spearman correlation (P-value)

[b] Categorical variables: Median (Interquartile Range)

Metabolic and Other Risk Factors:

Body mass index was associated with both ApoB and LDL-C in the younger groups, but not in the older cohort. As has been the case with other variables, ApoB demonstrated a stronger association with BMI (r=.332, p<.0001) than LDL-C (r=.246, p<.0001) in the younger cohort.

Diabetes status was associated with ApoB in the younger and older generation, whereas it was associated with LDL-C only in the older cohort. Smoking status was associated with ApoB in the younger cohort and with LDL-C in the older cohort. Systolic and diastolic blood pressure, measured as continuous variables, were associated with both ApoB and LDL-C in all age groups, except for systolic pressure in the older cohort. As for the presence of hypertension, both ApoB and LDL-C were associated with high blood pressure in the general and younger cohort. Hypertension seemed to have no influence on the variables of interest in the older generation.

Discussion and Conclusion

The aim of this study was to examine the distribution of ApoB and LDL-C across age groups and determine if ApoB demonstrated greater sensitivity to cardiovascular risk factors, as previous research has suggested. The general trend reinforced in our findings points towards ApoB acting as a more sensitive biomarker in relation to cardiovascular risk factors than LDL-C, mainly in the 17-50 cohort. All variables in which ApoB and LDL-C were both statistically significant in the younger cohort consistently revealed stronger associations with ApoB than LDL-C. In the senior cohort, the trends attenuated, and unlike their younger counterparts, if ApoB proved to be statistically significant, then LDL-C did, as well. ApoB does not seem to have a special relationship with risk factors in older age as it does with the young.

In addition, various risk factors demonstrated differential associations based on age. Race, diabetes status, and smoking status in particular were associated with serum ApoB in the younger cohort, but showed no statistically significant association with LDL-C. Conversely, race and diabetes status were associated with both ApoB and LDL-C in the older group. Hypertension, as defined in this study, also generated differential results based on age, with both ApoB and LDL-C responding stronger to high blood pressure (categorically and continuously) in younger adults than older adults.

Differences in lipoprotein distribution were evident between gender, race, and diabetes status. Whatever patterns found in the young were reversed in older age. The most plausible explanation of this phenomena could be attributed to the general pattern of mortality in old age. Higher risk groups present among the young could have died as age progressed, skewing the present distribution of lipoproteins among the senior population. As this study is cross-sectional in nature, we cannot account for risk over time nor can we come to conclusions about cardiovascular risk. Instead, we have sought to understand the relationship between lipoprotein biomarkers and cardiovascular risk factors. Cardiovascular risk in particular cannot be quantified nor qualified by a single factor. Rather, risk can be additive or even multiplicative.

Bachorik and colleagues (1997) highlight that ApoB and LDL-C follow a stepwise pattern of distribution across age, and that should be of particular concern when it comes to clinical practice. These lipoproteins mirror each other in trend – ApoB does indeed follow LDL-C. However, as our study shows, ApoB's amplified sensitivity to cardiovascular risk factors among the young falls in line with much of the recent consensus regarding ApoB's more sensitive role in CVD risk assessment and prevention efforts than LDL-C.

Strengths of our study include the large study population of adults with diverse demographic and metabolic characteristics. This allowed us to examine multiple facets of the association between ApoB, LDL-C, and cardiovascular risk factors. Weak points within this study center on its cross-sectional nature. Since we cannot follow-up with the subjects, we cannot deduce incidence nor actual risk. Moreover, we did not include information regarding lipid-lowering medication use in analysis due to a high proportion of missing values (not indicated in the tables). While this is a detriment, especially concerning the elderly, our findings are still germane in the context our aims, notwithstanding of the influence of medication. Future research efforts would certainly benefit from data concerning statin-use and other lipid-lowering prescriptions.

In brief, ApoB seems to have a special relationship with the younger cohort that does not manifest with LDL-C, and this relationship disappears in the older cohort. While the scope of this study does not allow us to make definitive conclusions as to the predictive ability of ApoB concerning CVD and CVD events, we have reason to believe that the assessment of CVD risk among the young would benefit from including ApoB in the already established battery of biomarkers.

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