Research Article

Apolipoprotein B as a Diagnostic and Therapeutic Marker for Coronary Artery Disease in South Asians

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ABSTRACT

Coronary Artery Disease (CAD) is one of the leading causes of mortality among South Asians, who represent only 25% of the global population but account for approximately 60% of CAD cases worldwide. This disparity is attributed to both genetic predispositions and lifestyle factors that contribute to an atypical lipoprotein profile, particularly characterized by elevated Apolipoprotein B (ApoB) levels. A systematic meta-analysis was conducted using six interventional studies published between 2004 and 2024, sourced from Google Scholar, PubMed, and Elicit, to evaluate the diagnostic and therapeutic potential of ApoB as a biomarker for CAD in South Asians. Results consistently demonstrated higher ApoB concentrations and ApoB mRNA expression in individuals with severe CAD. One study by Rychlik-Sych et al. reported that women requiring coronary artery bypass grafts had significantly elevated ApoB, while men exhibited a four-fold increase in ApoB gene expression. Additionally, research from the University of Kansas Medical Center identified specific APOA1 gene polymorphisms more prevalent in South Asians, contributing to lower HDL cholesterol levels and an increased ApoB/ApoA1 ratio—a strong predictor of cardiovascular risk. Despite its predictive value, ApoB remains underutilized in clinical settings. The discussion emphasizes the limitations of conventional lipid panels and argues for the integration of Apolipoprotein-100 tests and targeted therapies to enhance early detection and intervention. Ultimately, the study advocates for a shift toward ethnicity-specific cardiovascular care, where the inclusion of ApoB as a core biomarker could significantly reduce CAD burden in South Asian communities and lead to more equitable health outcomes.

Keywords: Apolipoprotein B, Diagnostic Marker, Therapeutic Marker, Coronary Artery Disease, South Asians

INTRODUCTION

CAD is a prevalent and widely diagnosed condition among the South Asian population (1), a demographic that encompasses individuals from Bangladesh, Bhutan, India, the Maldives, Nepal, Pakistan, and Sri Lanka (2). The main causes of CAD typically arise from atherosclerosis, a buildup of fats and cholesterol on the artery walls (3). According to the World Health Organization (WHO), although South Asians represent only 25% of the global population, they account for 60% of CAD patients worldwide (4). Moreover, South Asians tend to develop CAD up to 10 years earlier than the general population (5). This disparity is linked to a combination of factors,

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including diet, lifestyle, and genetics, with specific biomarkers in South Asians serving as significant indicators of the increased risk of CAD (6).

Biomarkers are measurable indicators of a biological condition or process. They can be molecules, genes, or characteristics that provide information about the state of health or disease in an organism.

In research, biomarkers are used to detect or predict disease progression, monitor treatment responses, or assess risk factors, making them essential tools in medical studies and clinical trials (7). A biomarker that is significantly under-researched and disproportionately reported in South Asians regarding the development of CAD is ApoB (8). ApoB is a primary protein component of atherogenic lipoproteins, including LDL, VLDL, and intermediate-density lipoprotein (IDL) (8). ApoB is a subsection of the more generic lipoprotein (8). Each ApoB-containing lipoprotein particle, such as LDL, VLDL, and IDL, has one molecule of ApoB (8). South Asians have a unique lipoprotein profile that includes high levels of triglycerides and higher Lipoprotein (a) (Lp(a)) levels than other ethnic groups (9). Lp(a) has emerged as a critical risk factor leading to the development of atherosclerotic plaque (9). Higher Lp(a) concentrations have been associated with an increased risk of various cardiovascular conditions, including ischemic CVD, aortic valve stenosis, and heart failure (9). While Lp(a) is an important risk factor, it represents a specific subset of lipoproteins and does not predict the total burden of atherogenic particles as comprehensively as ApoB. ApoB is a more efficient predictor of cardiovascular events and has been increasingly recommended in clinical guidelines for its superior predictive value (10). It was discovered that South Asians tend to carry a higher atherogenic burden than other ethnicities, as noted by higher levels of ApoB and LDL particles (11). This augments the vulnerability of South Asians to the onset of CAD, thereby representing a considerable health risk for this population.

I will be assessing how unique lipoprotein profiles within the South Asian community affect the expression of the ApoB biomarker, leading to CAD events.

METHODS

This systematic meta-analysis evaluated the role of ApoB in the development of CAD within the South Asian population by analyzing peer-reviewed interventional clinical studies published between 2004 and 2024.

Inclusion criteria required studies to involve South Asian populations, be clinical trials or interventional in nature, be published in English, and include data on ApoB levels or its association with CAD. Studies were excluded if they focused on cardiomyopathy or unrelated heart failure, involved participants under 18, were animal/pre-clinical studies, or were secondary research, such as reviews or meta-analyses.

The search was conducted using PubMed, Google Scholar, and Elicit—an AI-powered tool designed to identify relevant academic literature. Key search terms included "South Asians," "coronary artery disease," "lipoprotein testing," "Apolipoprotein B," "genetic variation," and "adverse heart conditions." After screening over 40 articles, six interventional studies that met all inclusion criteria were selected for in-depth analysis. These studies were assessed for their specific relevance to ApoB and CAD in South Asians, as seen in Table 1.

RESULTS/DISCUSSION

CAD in the South Asian Community

Assessment of Prevalent CAD Risk Factors in the South Asian Population. The lipoprotein profile of South Asians exhibits a marked distinction from that of other global populations. This difference is often characterized by dyslipidemia, which refers to an imbalance of lipids in the blood (12). Dyslipidemia is characterized by elevated triglyceride levels, reduced high-density lipoprotein (HDL) cholesterol, increased lipoprotein(a) levels, and a higher burden of atherogenic particles, despite similar low-density lipoprotein cholesterol levels compared to other ethnic subgroups (11). This is illustrated in a study published by the *Global Heart* as a part of the "Center for Cardiometabolic Risk Reduction in South Asia" (CARRS) project. The data for the South Asian cohort came from the CARRS study, while the data for U.S. groups were sourced from the National Health and Nutrition Examination Survey (NHANES). The researchers in this study aimed to investigate dyslipidemia within different Body Mass Index (BMI) ranges across multiple ethnic groups. Data from 8,448 resident South Asians, 274 U.S. Asians, 404 U.S. Blacks, 308 U.S. Hispanics, and 703 U.S. Whites without previously known diabetes were analyzed. Among individuals with a normal BMI (defined as 18.5 to 24.9 kg/m^2), the prevalence of combined dysglycemia and dyslipidemia was 33% in men and 11% in women for South Asians, compared to 15% and 1% for U.S. Asians, 5% and 2% for U.S. Blacks, 11% and 2% for U.S. Hispanics, and 8% and 2% for U.S. Whites (13).

Adjusted models showed that, compared to U.S. Whites, South Asians were more likely to exhibit

both dysglycemia and dyslipidemia across all BMI categories in men and at a BMI of 18.5 to 29.9 in women (13). As visualized in Table 2, there is an extremely pronounced difference in the percentages of dysglycemia and dyslipidemia between South Asians and other populations. For instance, dysglycemia and dyslipidemia were more than four times higher in South Asians (combined men and women: 44%) than it was in Caucasians (combined men and women: 10%). This is a direct example of how the unique lipoprotein profile within the South Asian community dramatically increases the risk for CAD, Acute Myocardial Infarction (AMI), Peripheral Artery Disease, Insulin Resistance, and Cartoid Artery Disease (14).

Lipoprotein Indicators and Sensitivity for Addressing CAD. While pre-existing conditions, dietary habits, and lifestyle factors are key contributors, specific biomarkers like Apolipoprotein A and B (ApoA and ApoB) have emerged as more reliable indicators of CAD risk in this population (15). These biomarkers offer high predictive accuracy and can be measured consistently, providing crucial data for tracking disease progression (15). The sensitivity of such biomarkers may pave the way for targeted treatments and interventions. However, it is essential to analyze how personal and cultural choices impact CAD risk within South Asians' unique lipoprotein profiles, laying the foundation for discussing biomarker expression.

Lifestyle and Adaptation

CAD is generally the result of specific lifestyle choices that an individual inadvertently makes throughout their life without knowing the long-term consequences that it can have on the human body. Some of these lifestyle choices include physical inactivity, smoking habits, and eating a large amount of saturated fat (16). In an article by the American Journal of Cardiology, a comprehensive case-control study compared 4,000 South Asians from five countries with 23,000 participants from non-South Asian countries (17). They found that South Asians had fewer protective lifestyle factors, such as lower fruit and vegetable intake, less physical activity, and increased

Table 2. Dyslipidemia Percentages Under Normal BMI By Sex Across Ethnic Groups (13)

Ethnic Group (n)	**Incidence of Dyslipidemia** Men (%)	**Incidence of Dyslipidemi** Women (%)
South Asians (8,448)	33%	11%
U.S Asians (274)	15%	1%
U.S Blacks (404)	5%	2%
U.S Hispanics (308)	11%	2%
U.S Whites (703)	8%	2%

Table 1. Summary Table of Selected Studies

Study	Population	Key Findings
CARRS vs. NHANES Study (Patel *et al*., 2016)	8,448 South Asians, 1,689 non-South Asians (U.S. groups (Asians, Blacks, Hispanics, Whites))	South Asians with normal BMI showed a higher prevalence of dysglycemia and dyslipidemia, suggesting ApoB's role in CAD risk.
INTERHEART Study (Yusuf *et al*., 2004)	4,000 South Asians, 23,000 non-South Asians	South Asians exhibited fewer protective lifestyle factors and higher intake of atherogenic foods, linking ApoB to CAD.
MASALA Study (Kanaya *et al*., 2014)	South Asian immigrants in the U.S.	High prevalence of hypertension and T2DM in South Asians, with dyslipidemia indicating ApoB's significance.
ApoB Expression Study (Rychlik-Sych *et al*., 2023)	110 Polish patients undergoing coronary interventions	Elevated ApoB levels in patients requiring PCI/CABG suggest its utility as a marker for CAD severity.
APOA1 Gene Polymorphism Study (Singh *et al*., 2012)	94 South Asian immigrants in the U.S.	Specific APOA1 gene polymorphisms in South Asians contribute to lower HDL cholesterol and increased CAD risk, with ApoB as a key marker.
Lipoprotein(a) Reduction Study (Tsimikas *et al*., 2019)	Patients with elevated lipoprotein(a) levels	Antisense therapy and PCSK9 inhibitors significantly lowered lipoprotein(a) levels, reducing CAD risk.

intake of sodium (17). Additionally, it was discovered that South Asians commonly consume high amounts of saturated fats and refined carbohydrates, including ghee, fried foods, potatoes, white rice, and sugary drinks (17). Lacto-vegetarian and ovo-lacto-vegetarian South Asians often eat calorie-dense foods like ghee, butter, and cream, which are linked to atherogenic dyslipidemia, high BMI, and atherosclerotic cardiovascular disease (ASCVD) (17). Non-vegetarian South Asians also experience obesity and dyslipidemia due to high intake of animal products and refined carbohydrates (17).

In addition to the South Asian population at large, a smaller yet often overlooked subgroup consists of South Asian immigrants who have relocated abroad. These individuals, having adapted to Western environments and lifestyles, face an increased risk of developing CAD (17). This population is particularly unique, as the contrast between their traditional lifestyles and the adopted ones reveals clear indicators of how CAD risk develops. The relationship between cultural changes and newly emerging health issues, which ultimately contribute to CAD events, is especially pronounced in this group. The MASALA Study (Mediators of Atherosclerosis in South Asians Living in America) is one of the most renowned organizations whose sole purpose is to bridge the gap in understanding of this widespread problem (18). In a study conducted by MASALA researchers, hypertension was found in 43% of the men and 35% of the women. South Asian immigrants also have a two-fold to four-fold increased prevalence of T2DM (Type 2 Diabetes Mellitus). In fact, 33% of the participants in the study had pre-diabetes, and 25% had T2DM. They also discovered that dyslipidemia has an attributable risk of 49.2%, which connects directly with the diverse lipoprotein profile characterized by elevated cholesterol levels and atherogenic burden mentioned earlier in this paper (17). It is vital to understand how health conditions like hypertension and type 2 diabetes interrelate, as these conditions commonly contribute to the development of CAD in this population. The increased probability and ubiquity of these conditions, coupled with the major diet and lifestyle changes associated with the immigrant population, act as a major driver of CAD events. This analysis underscores the severity of CAD and other conditions prevalent in the South Asian population. While personal choices play a role in these conditions, the underlying genetic predisposition within this group is equally important. Consequently, biomarkers such as various lipoproteins and ApoB emerge as key indicators, whose expression provides valuable insights into the causes of cardiac events and associated genetic factors.

ApoB Expression

ApoB Expression in CAD. Biomarkers are objective measurements of what is happening in our bodies at a given moment. ApoB is a biomarker used to predict cardiovascular disease risk. This is due to its ability to measure the number of atherogenic particles in the blood, including LDL receptors, chylomicrons, and even ApoA (19). Traditional cholesterol markers only provide information about the total amount of cholesterol in the blood. When examining South Asian cholesterol levels as a whole, we can see that they are at a higher level in comparison to other ethnicities (20). This is indicated in a report by the American Heart Association, which discovered that 29.2% of Asian men and 25% of Asian women have LDL levels above 130, which can have adverse effects on heart health (20).

The prediction, measurement, and even potential mitigation of such conditions come directly from biomarkers. When looking at cholesterol from a more microscopic point of view, we can see that the expression of biomarkers such as ApoB and ApoA is a major indicator of premature CAD (21). In a study conducted by Mariola Rychlik-Sych, PhD, she and her team explored the role of ApoB as a marker of cardiovascular disease (CVD) by examining its concentration in 110 participants from a single center in Poland. The study found that women requiring percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) had significantly higher ApoB levels compared to those who did not, indicating its significant role as a marker for atherosclerosis severity. Similarly, men requiring PCI/CABG showed a four-fold increase in ApoB expression at the mRNA level compared to those without coronary plaques (22). Table 3, below, further illustrates this relationship and compares the ApoB concentration of patients requiring PCI/CABG (group A) and patients who were not eligible for coronary angioplasty due to atheromatous plaques and those in whom no stenoses were found (groups B and C). As visualized in Table III (Appendix A), group A had significantly higher levels of ApoB concentration and increased expression at the mRNA level (22).

Although the research was conducted within a diverse population rather than being specific to South Asians, it emphasizes the utility of ApoB levels as a robust predictor of CAD across various demographic groups. This finding is particularly pertinent for the South Asian population, where ApoB levels are irregularly elevated, as seen by the studies above. Consequently, the significance of ApoB as a determinant of CAD in the general population suggests that it could serve as a valuable marker for assessing CAD

Table 3. ApoB Concentration for Patients Requiring PCI/ABG Versus Healthy Controls (22)

Parameter PCI/ABG Group: Red Control Group: Blue	Patients after PCI or referred for CABG: group A (n = 54)	Patients with no history of PCI/CABG: groups B and C (n = 56)	Patients after PCI or referred for CABG: group A (n = 54)	Patients with no significant lesions in the coronary arteries: group C (n = 43)
ApoB concentration, μg/ml, median (IQR)	10.4 (6.18–13.19)	7.93 (4.91–11.96)	10.4 (6.18–13.19)	7.09 (4.23–10.73)
Increase in the **APOB** expression at the mRNA level	**1.28-fold**	–	**1.53-fold**	–

Abbreviations: CABG, coronary artery bypass grafting; IQR, interquartile range; PCI, percutaneous coronary intervention.

risk within the South Asian cohort.

Apolipoprotein A-1 Gene Polymorphisms and Their Association with Apo B. When looking at ApoB in LDL, it is important to consider apolipoprotein A1 (ApoA-1), which is the primary component of HDL (23). Elevated ApoB and decreased ApoA-1 are associated with an increased risk of cardiovascular disease (23). Specifically, regarding ApoA-1, we can examine gene polymorphisms. Polymorphisms refer to the presence of two or more variant forms of a specific DNA sequence that can occur among different individuals or populations (24). In the context of the ApoA-1 gene, these polymorphisms can affect how well the ApoA-1 protein functions or how it is produced. Such variations can influence HDL cholesterol levels and, consequently, impact cardiovascular risk (25).Notably, a considerable part of the unique South Asian lipoprotein profile that affects the expression of ApoB and ApoA-1 comes from gene polymorphisms (26). APOA1 (which encodes ApoA-1) gene polymorphisms within the South Asian immigrant population living in the United States were studied at the University of Kansas Medical Center. Researchers analyzed the DNA of 94 South Asian adults and identified specific variations in the APOA1 gene, particularly in three gene polymorphisms: T655C, T756C, and T1001C (26). These variations affect the gene's function and are associated with lower levels of beneficial HDL cholesterol. The study revealed that South Asians have a unique distribution of these variations compared to other populations, with notably higher frequencies of the T655C and T1001C polymorphisms (26). This unique genetic pattern may contribute to their increased risk of heart disease. This highlights that the risk of heart disease among South Asians involves factors beyond just lifestyle and diet, pointing to additional underlying contributors to their susceptibility. The analysis of ApoB, ApoA1 gene polymorphisms, and their patterns in dyslipidemia highlights how genetic profiles influence biomarkers associated with CAD risk in South Asians. This area of research remains very underexplored, with many attributing CAD primarily to lifestyle factors. Addressing the genetic component of CAD is crucial, as understanding the lipoprotein profile of South Asians through biomarkers like ApoB and ApoA1 can enhance strategies for cardiac health. Ongoing advancements and emerging technologies are already fostering significant progress in this domain, promising more tailored and effective approaches for improving cardiovascular health.

Future Implications

ApoB in Therapeutic Intervention. Cardiology is a dynamic and rapidly evolving field, characterized by continuous advancements and discoveries. Each day brings new treatments, insights into conditions, and breakthroughs, driving substantial progress and innovation in this specialty. Research that focuses on why South Asians are disproportionately affected by CAD has accounted for only a small portion of research. Bringing awareness to this issue is critical, and scientists and researchers are already beginning to formulate hypotheses surrounding different trends that are evident across various ethnic populations. In the specific case of CAD within South Asians, biomarkers, such as ApoB, as well as newly created therapies, are leading to a more accurate prediction and potential cure for CAD within this demographic (27). Notably, gene polymorphisms like APOA1 help us better understand the causes of CAD risk and the development of effective preventive strategies. Additionally, antisense therapy is conventionally defined as a genetically based drug design for the therapeutic administration of short single-stranded DNA or RNA polymers (i.e., antisense oligonucleotides) synthesized in

vitro, which regulate gene expression by binding target RNA molecules in a sequence-specific manner (28). This therapy has been identified as a potential therapy in reducing lipoprotein (a) concentrations. This directly intersects with ApoB as well as ApoA, since they are all interconnected with the lipid profile as a whole. A study conducted by Dr. Tsimikas, a professor and MD at UC San Diego Health, and colleagues conducted a trial to evaluate the effectiveness of an antisense oligonucleotide targeting lipoprotein(a) messenger RNA. The study revealed that antisense therapy significantly reduces lipoprotein(a) levels (29). Additionally, researchers observed that alirocumab, a PCSK9 inhibitor, decreases cardiovascular events by lowering lipoprotein(a), independent of its effect on LDL-C levels. These trials could introduce a new strategy for reducing cardiovascular disease and CAD risk across a variety of populations (29).

ApoB Testing for Preventive Care. While the above discussion primarily emphasizes intervention, prevention is equally crucial in mitigating the global spread of heart disease. Alongside targeted therapies and specific gene patterns, understanding the predictive value of various biomarkers and proteins plays a vital role in this effort. Specifically, ApoB has been the main discussion point throughout this paper. This is the most straightforward and reliable metric that has been clinically proven to assess risk in patients (15). According to Cleveland Clinic, the Apolipoprotein B-100 test is a blood test that can evaluate heart disease risk by measuring the amount of ApoB (30). In fact they stated that measuring Apo B can predict heart disease and blood vessel sicknesses better than the standard lipid panel (30). This is because each ApoB molecule carries LDL, which provides an accurate count as a result of the one-to-one ratio (30). Apolipoprotein B-100 levels typically range from 20 to 400 mg/dL (30). A normal level is 66 to 133 mg/dL for men and 60 to 117 mg/dL for women, with higher levels indicating an increased risk of heart and blood vessel disease (30). Additionally, independent laboratories in the US provide this test at a cost of $50-100, and it is typically covered by insurance, making it highly accessible and affordable. This approach could significantly benefit the South Asian population by enabling early prediction of CAD. Implementing ApoB testing in third-world countries could serve as a powerful tool in combating this global issue. By combining intervention with prevention, focusing on ApoB levels, gene polymorphisms, and targeted therapies, we could revolutionize the management of CAD in South Asians, paving the way for ethnicity-based healthcare advancements.

Limitations

One limitation of this study is the inclusion of key studies that primarily focus on non-South Asian populations, which could influence the generalizability of findings specific to South Asians. While the studies provide valuable insights into the role of ApoB and CAD, differences in lifestyle, genetic predispositions, and environmental factors between South Asian and non-South Asian populations may impact the applicability of these results. Despite this, the studies are relevant as they offer a foundation for understanding the broader mechanisms of CAD and highlight the importance of considering ethnicity-specific risk factors. The absence of a significant number of South Asian participants in the studies examined underscores how the population is understudied and underrepresented in research regarding CAD. Future research focusing on South Asian populations will be essential for confirming and refining these findings within this group.

CONCLUSION

The varied lipoprotein profiles characteristic of the South Asian population are marked by dyslipidemia, an elevated atherogenic burden, and increased lipoprotein (a) concentrations. These factors contribute to the heightened expression of the ApoB biomarker, largely driven by gene polymorphisms. The elevated ApoB levels, coupled with corresponding cholesterol spikes, significantly amplify the susceptibility of South Asians to cardiac conditions such as CAD. This issue is further exacerbated by lifestyle adaptations, particularly among South Asian immigrants who have adopted Western habits, compounding their cardiovascular risks.

However, the predictive power of ApoB presents a promising opportunity to counteract these trends. ApoB stands out as a reliable early indicator of CAD, particularly within the South Asian population. The Apolipoprotein B-100 test offers a more precise assessment of blood vessel health than standard lipid panels, enabling earlier and more accurate detection of cardiovascular risks.

Beyond individual diagnosis, raising awareness about the increased prevalence of CAD within the South Asian population is critical. Proactive efforts to address these disparities, especially in third-world countries where healthcare resources may be limited, could lead to significant improvements in global health outcomes. The persistent issue of CAD among South Asians now has a viable pathway for both prevention and intervention. By leveraging the powerful diagnostic potential of the ApoB

biomarker and advocating for its use as a therapeutic target towards the unique South Asian lipoprotein profile, we can make meaningful strides in reducing the burden of CAD within this vulnerable population.

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