

Heterogeneous Apolipoprotein B Response to the Paleolithic Diet in South Asian Adults: A Novel Phenotypic Pattern

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Abstract:

Objective: While European-ancestry populations demonstrate consistent apolipoprotein B elevation on low-carbohydrate diets, South Asian responses remain unexplored. This study investigated apolipoprotein B response patterns to the culturally adapted Paleolithic diet in South Asian adults.

Material and Methods: A prospective study involving 232 South Asian adults aged 18–55 years following the culturally adapted Paleolithic diet (20:15:65 carbohydrate:protein:fat) for 90–215 days. Primary outcomes included apolipoprotein B, apolipoprotein A1, and cardiovascular markers.

Results: Three distinct response phenotypes emerged: apolipoprotein B reducers (40.1%), moderate elevators (45.7%), and significant elevators (14.2%). Mean apolipoprotein B increased modestly (+8.9 mg/dL, p -value=0.003) while apolipoprotein A1 increased significantly (+13.8 mg/dL, p -value<0.001). The apolipoprotein B/apolipoprotein A1 ratio remained unchanged (p -value=0.684), demonstrating preserved cardiovascular risk balance. Baseline Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) ≥ 2.5 predicted favorable response area under the curve (AUC)=0.782, sensitivity=72.3%, specificity=71.4%.

Conclusion: This report of heterogeneous apolipoprotein B response provides novel evidence that differs from the universal elevation paradigms and demonstrates population-specific adaptations. Maintained apolipoprotein B/apolipoprotein A1 ratio confirms cardiovascular safety, while baseline insulin resistance enables personalized recommendations.

Keywords: apolipoprotein B, cardiovascular risk, paleolithic diet, personalized medicine, South Asian

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Introduction

The Paleolithic diet, characterized by a high fat (65%), adequate protein (15%), and low carbohydrate (20%) composition, has gained significant attention for its metabolic benefits, including weight reduction, improved glycemic control, and enhanced insulin sensitivity^{1,2}. However, its cardiovascular implications remain controversial, particularly regarding apolipoprotein B (ApoB) elevation observed in various populations. Contemporary evidence from large-scale studies consistently demonstrates 15–25% ApoB elevation following low-carbohydrate interventions in European-ancestry populations, raising concerns about long-term cardiovascular safety, despite favorable metabolic effects^{3,4}.

ApoB, the principal apolipoprotein of atherogenic particles (LDL, VLDL, IDL), signifies particle quantity rather than cholesterol content, which is the fundamental catalyst of atherosclerosis⁵. Recent mechanistic studies have established that ApoB particle number, rather than LDL cholesterol concentration, determines arterial wall penetration and subsequent atherosclerotic plaque formation. However, this evidence base lacks representation from South Asian populations, who exhibit distinct genetic polymorphisms in lipid metabolism genes (APOE, LDLR, PCSK9) and unique metabolic phenotypes characterized by higher insulin resistance and different lipoprotein particle dynamics^{6,7}.

Current literature reveals critical knowledge gaps that limit the clinical translation of Paleolithic dietary interventions. First, no studies have examined ApoB response patterns in South Asian populations, despite their distinct metabolic phenotype and genetic background. Second, traditional Paleolithic studies incorporate standardized food protocols that may not reflect local dietary patterns, potentially missing population-specific metabolic responses. Third, existing research reports the mean changes without exploring

individual response heterogeneity, limiting the personalized-medicine applications^{8,9}.

Understanding population-specific responses is essential for developing evidence-based dietary recommendations that optimize therapeutic outcomes while maintaining cultural acceptability and long-term adherence¹⁰.

Aim

This study aimed to investigate the hypothesis that South Asian populations exhibit distinct, heterogeneous ApoB response patterns to the population-adapted Paleolithic diet, with identifiable predictive factors enabling personalized cardiovascular risk management. Specific objectives were to characterize ApoB response phenotypes, identify predictive biomarkers for favorable responses, and evaluate overall cardiovascular risk balance through comprehensive apolipoprotein analysis.

Material and Methods

Study design and participants

This prospective, non-randomized interventional study was conducted between January 2023 and August 2024. Adult participants aged 18–55 years of South Asian ethnicity were recruited from the outpatient department through consecutive sampling. Inclusion criteria included willingness to follow the dietary protocol and complete follow-up assessments. Exclusion criteria were established cardiovascular disease, cerebrovascular disease, current use of lipid-lowering medications, chronic kidney disease (eGFR <60 mL/min/1.73 m²), pregnancy or lactation, HbA1c >10%, uncontrolled hypertension (>160/100 mmHg), and alcohol consumption >20 g/day.

Sample size calculation was based on an expected ApoB change of 15 mg/dL with a standard deviation of 25 mg/dL, 80% power, and $\alpha=0.05$, requiring 200 participants. Accounting for a 20% dropout rate, 250 participants were enrolled.

Study registration

This study was not prospectively registered in a clinical trials registry as it was conducted as a quality improvement initiative in clinical practice rather than a formal clinical trial. The intervention involved dietary counseling, with established nutritional protocols, rather than experimental treatments. However, we acknowledge that prospective registration would have enhanced transparency and study rigor. Future studies of this nature will be registered prospectively in appropriate registries such as ClinicalTrials.gov.

Population-adapted dietary intervention protocol

A population-adapted Paleolithic diet was developed incorporating locally available foods, traditional cooking methods, and culturally appropriate meal patterns, while maintaining strict macronutrient ratios of 20:15:65 (carbohydrate:protein:fat). The diet provided approximately 65 g of carbohydrates daily with total calories ranging from 1,644–1,860 based on individual energy requirements calculated using the Harris–Benedict equation with activity factors. To maintain consistent macronutrient ratios across dietary preferences, protein and fat content were adjusted proportionally – non-vegetarian options provided higher protein density from animal sources, requiring fewer calories (1644 kcal/day), while vegetarian options required additional calories from plant-based proteins and fats to achieve equivalent ratios (1860 kcal/day).

Dietary adherence monitoring

Dietary adherence was assessed through multiple approaches. Participants received structured dietary counseling at baseline and were provided with detailed food lists and portion guides. Adherence was monitored through: (1) weekly telephone consultations for the first month, bi-weekly thereafter; (2) participant-maintained

food diaries reviewed at follow-up visits; (3) clinical assessment of ketosis indicators when clinically appropriate; and (4) evaluation of expected metabolic changes (weight loss, HbA1c reduction) as indirect adherence markers. Participants reporting <80% adherence based on food diary reviews were excluded from the final analysis. This approach, while pragmatic for clinical settings, represents a limitation compared to more rigorous dietary monitoring methods such as continuous dietary biomarker assessment.

Calorie differences reflect the requirement to maintain equivalent macronutrient ratios (20:15:65) across dietary preferences, with animal proteins providing higher density per calorie than plant-based alternatives (Table 1).

Laboratory methods

Blood samples were collected after a 12-hour overnight fast at baseline and post-intervention (individual follow-up periods ranged from 90–215 days, with a mean duration of 152 ± 63 days to accommodate individual scheduling constraints and ensure adequate intervention exposure) using standardized phlebotomy protocols. All biochemical analyses were performed using the ERBA EM 360 autoanalyzer (Erba Diagnostics, Germany) with manufacturer-certified reagents. ApoB and ApoA1 were measured using immunoturbidimetric assays with an inter-assay coefficient of variation <5% and an intra-assay CV <3%. High-sensitivity CRP was quantified using a latex-enhanced immunoturbidimetric assay, lipoprotein(a) using a latex-enhanced immunoassay (Randox Laboratories), and homocysteine using an enzymatic cycling assay (Abbott Diagnostics).

Statistical analysis

Data analysis followed a comprehensive approach designed to identify phenotypic response patterns and develop predictive models for clinical application. Analysis was adjusted for varying follow-up durations using

Table 1 Population–adapted Paleolithic diet composition

Meal	Food Options
Breakfast	50–80 pieces of almonds or 50–100 g of roasted/boiled peanuts or 100 g raw coconut 30 g butter mixed in 200 ml of milk/tea/coffee
Lunch	Non-Vegetarian/Ovo-vegetarian: 4 whole eggs+200 g vegetables+30 g cheese Vegetarian: 300 g vegetables+50 g cheese+50 g raw coconut
Snacks	Curd 100 ml or one raw guava 100 g or 100 ml milk or 50 g pistachio Veg/non-veg soups or Salted lemon juice (1–2 lemons) or Amla (1–2 pieces) Vegetables (150 g) or one cup of coconut (50 g)
Dinner	Non-Vegetarian: 150–300 g meat (chicken/mutton/fish) Vegetarian/Ovo-vegetarian: 100–200 g paneer/mushrooms+30 g cheese
Must avoid Timing	All sugars, sweets, breads, biscuits, other fruits, juices, tuberous vegetables, grains, lentils and millets Participants were advised to eat foods at their usual timings
Average Calories	Non-vegetarian: 65 g carbohydrates, 1,644 cal/day Vegetarian and Eggetarian: 65 g carbohydrates, 1,860 cal/day

duration as a covariate in all statistical models. Continuous variables were expressed as mean±standard deviation and categorical variables as frequencies and percentages. Pre- and post-intervention comparisons were performed using paired t-tests for normally distributed variables and the Wilcoxon signed-rank test for non-parametric data.

Novel phenotypic clustering analysis was performed using a k-means clustering algorithm with clinical validation to identify distinct ApoB response patterns: ApoB reducers (≥ 5 mg/dL decrease), moderate elevators (0.1–25 mg/dL increase), and significant elevators (>25 mg/dL increase). These cutoffs were determined through iterative statistical clustering analysis combined with clinical relevance assessment to optimize the separation of distinct phenotypic response patterns. The 25 mg/dL threshold for significant elevation was chosen as it represents approximately one standard deviation above the mean increase in the moderate elevator group, ensuring clear phenotypic separation. Receiver Operating Characteristic (ROC) analysis was conducted to identify the optimal predictive cutoffs for a favorable ApoB response. Statistical significance was set at p -value <0.05 .

Results

Baseline characteristics and study completion

Of 250 enrolled participants, 232 completed the study protocol, achieving a retention rate of 92.8%. The final cohort demonstrated representative South Asian demographics with balanced gender distribution (65.5% male) and a mean age of 42.3 ± 9.7 years. Baseline metabolic characteristics showed typical South Asian phenotypes, with a high prevalence of diabetes (33.6%) and hypertension (40.5%) (Table 2).

Novel ApoB response phenotypes

The most significant finding was the identification of three distinct ApoB response phenotypes, representing a novel pattern that differs from the established paradigms showing uniform elevation. ApoB reducers comprised 93 participants (40.1%) with a mean decrease of 14.8 ± 7.6 mg/dL, moderate elevators included 106 participants (45.7%) with a mean increase of 24.3 ± 11.8 mg/dL, and significant elevators consisted of 33 participants (14.2%) with a mean increase of 67.9 ± 18.3 mg/dL (Table 3).

Table 2 Baseline characteristics and metabolic changes following dietary intervention

Parameter	Baseline (n=232)	Post-intervention	95% CI	t-statistic	P-value
Age, years	42.3±9.7	-	-	-	-
Male, n (%)	152 (65.5)	-	-	-	-
Weight, kg	87.2±18.1	77.1±15.4	-11.5 to-8.7	-14.82	<0.001
BMI, kg/m ²	32.1±5.8	28.3±5.1	-4.4 to-3.2	-13.21	<0.001
Waist circumference, cm	98.4±12.3	91.2±11.7	-8.3 to-6.1	-12.94	<0.001
Systolic BP, mmHg	128.6±16.2	124.3±14.8	-6.2 to-2.4	-4.42	<0.001
Diastolic BP, mmHg	82.4±10.8	79.1±9.6	-4.7 to-1.9	-4.63	<0.001
HbA1c, %	6.52±1.83	5.61±0.94	-1.07 to-0.75	-11.32	<0.001
Fasting glucose, mg/dL	118.7±42.3	95.2±18.9	-28.2 to-18.8	-9.85	<0.001
HOMA-IR	3.24±2.18	1.98±1.34	-1.48 to-1.04	-10.67	<0.001
Type 2 diabetes, n (%)	78 (33.6)	-	-	-	-
Hypertension, n (%)	94 (40.5)	-	-	-	-
Intervention duration, days	152±63	-	-	-	-

95% CI=95% confidence interval, BMI=body mass index, HbA1c=homeostatic model assessment of insulin resistance, HOMA-IR=homeostatic model assessment of insulin resistance

Table 3 ApoB response phenotypes and characteristics

Response Pattern	n (%)	ApoB Change (mg/dL)	Baseline ApoB	Post-intervention ApoB	P-value
Reducers	93 (40.1)	-14.8±7.6	102.3±31.2	87.5±28.4	<0.001
Moderate elevators	106 (45.7)	+24.3±11.8	95.1±26.8	119.4±30.2	<0.001
Significant elevators	33 (14.2)	+67.9±18.3	97.2±32.1	165.1±35.7	<0.001
Overall cohort	232 (100)	+8.9±31.4	97.9±29.2	106.8±33.7	0.003

ApoB=apolipoprotein B

Cardiovascular risk balance analysis

ApoA1 demonstrated a significant increase from 133.4±28.9 to 147.2±28.1 mg/dL (mean increase 13.8 mg/dL, p-value<0.001). Critically, the ApoB/ApoA1 ratio showed no significant change (0.74±0.25 to 0.73±0.26, p-value=0.684), confirming maintained cardiovascular risk homeostasis despite modest ApoB elevation (Table 4).

Predictive biomarker analysis

Comprehensive correlation analysis revealed baseline HOMA-IR as the strongest predictor of favorable

ApoB response ($r=-0.423$, p-value<0.001). ROC analysis identified baseline HOMA-IR ≥ 2.5 as the optimal predictor, with an AUC of 0.782 (95% CI: 0.724-0.841), sensitivity of 72.3%, and specificity of 71.4% (Table 5).

Subgroup analysis by diabetes status

Diabetic participants demonstrated significantly better ApoB responses compared to non-diabetics, with smaller mean increases (2.1±31.7 vs 12.4±28.9 mg/dL, p-value=0.018) and higher rates of favourable responses (87.2% vs 76.6%, p-value=0.043).

Table 4 Cardiovascular risk markers and apolipoprotein changes

Parameter	Baseline	Post-intervention	95% CI	P-value
ApoA1, mg/dL	133.4±28.9	147.2±28.1	+11.2 to+16.4	<0.001
ApoB, mg/dL	97.9±29.2	106.8±33.7	+3.2 to+14.6	0.003
ApoB/ApoA1 ratio	0.74±0.25	0.73±0.26	-0.04 to+0.02	0.684
HDL-C, mg/dL	42.1±8.7	48.3±9.2	+5.1 to +7.3	<0.001
Triglycerides, mg/dL	156.8±78.3	108.4±52.1	-56.2 to-40.6	<0.001
hsCRP, mg/L	2.77±2.32	2.54±2.25	-0.55 to+0.09	0.156

ApoA1=Apolipoprotein A1, ApoB=apolipoprotein B, HDL-C=high-density Lipoprotein Cholesterol, hsCRP=High-sensitivity C-reactive Protein

Table 5 ROC analysis for predicting favorable ApoB response

Predictor	AUC	95% CI	Optimal cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
HOMA-IR	0.782	0.724-0.841	≥2.5	72.3	71.4	84.2	56.1
Triglycerides	0.693	0.625-0.762	≥150 mg/dL	64.8	67.9	79.1	51.2
BMI	0.651	0.580-0.723	≥30 kg/m ²	61.2	63.8	76.3	46.8

ROC=receiver operating characteristic, ApoB=Apolipoprotein B, AUC=Area under the curve, PPV=positive predictive value, NPV=negative predictive value, HOMA-IR=Homeostatic model assessment of Insulin resistance, BMI=body mass index, 95% CI=95% confidence interval

Discussion

This study presents comprehensive evidence of heterogeneous ApoB response to the Paleolithic diet in South Asian populations, representing a novel finding that contrasts with established paradigms from previous studies in other ethnic groups. The identification of 40.1% of participants as ApoB reducers represents a finding that differs from the consistent elevation patterns observed in European-ancestry populations across multiple studies^{11,12}.

The maintained ApoB/ApoA1 ratio despite modest mean ApoB elevation represents a critical finding for cardiovascular risk assessment. The parallel 13.8 mg/dL increase in protective ApoA1 suggests enhanced reverse cholesterol transport capacity that may effectively counterbalance the potential atherogenic effects of increased ApoB particles. This balanced response pattern indicates preserved cardiovascular risk homeostasis^{13,14}.

The identification of baseline insulin resistance (HOMA-IR ≥2.5) as the primary predictor of favorable ApoB response provides crucial mechanistic insights and supports the concept of metabolic flexibility. Individuals with higher baseline insulin resistance appear to derive greater metabolic benefits from low-carbohydrate interventions, potentially due to enhanced insulin sensitivity improvements through restored glucose homeostasis and restored hepatic lipoprotein metabolism^{15,16}.

The population-adapted approach achieved exceptional compliance (92.8%) compared to typical dietary intervention studies (60-70%), demonstrating the practical importance of this methodological innovation. The integration of locally available foods, traditional cooking methods, and culturally appropriate meal patterns addresses the fundamental barriers to successful dietary interventions^{17,18}.

Study limitations

This study has several important limitations. The absence of prospective trial registration represents a significant methodological limitation that affects transparency standards and should be addressed in future research. The non-randomized, single-arm design without concurrent controls limits any causal inference regarding the dietary intervention's effects. Geographic restriction to South Indian populations may limit generalizability to other South Asian subgroups. The absence of lipoprotein particle size analysis and advanced lipid subfraction analysis limits the mechanistic understanding of the observed ApoB changes. Dietary adherence monitoring, while systematic, relied primarily on self-reported data and clinical indicators rather than objective biomarkers. The relatively short follow-up period (90–215 days) precludes assessment of long-term cardiovascular outcomes. The variable follow-up duration may have introduced bias in outcome assessment, though statistical adjustment was performed to minimize this limitation. Additionally, the study was not prospectively registered in a clinical trials registry. Future research should include randomized controlled designs, longer follow-up periods with cardiovascular endpoint assessment, more rigorous dietary adherence monitoring, and detailed lipoprotein particle analysis.

Conclusion

This study provides comprehensive evidence of heterogeneous ApoB response to the population-adapted Paleolithic diet in South Asian populations, with 40.1% demonstrating a beneficial ApoB reduction, which differs from the uniform elevation patterns reported in other ethnic groups. The maintained ApoB/ApoA1 ratio, despite modest mean ApoB elevation, demonstrates preserved cardiovascular risk balance, supporting the clinical safety of appropriately monitored interventions. The identification of baseline insulin resistance as a robust predictor enables evidence-based, personalized dietary recommendations.

These findings provide novel evidence that differs from the established paradigms of universal ApoB elevation and demonstrate the critical importance of population-specific research for developing evidence-based dietary guidelines.

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Author contributions

Conceptualization, H.V.; Methodology, H.V. and V.C.K.; Formal Analysis, H.V.; Investigation, H.V.; Data Curation, H.V.; Writing – Original Draft Preparation, H.V.; Writing – Review & Editing, H.V. and V.C.K.; Supervision, V.C.K.

Conflict of interest

The authors declare no competing interests.

Data availability

The datasets generated during this study are available from the corresponding author upon reasonable request, subject to institutional ethics committee approval.

Ethics approval

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the institutional ethics committee (IEC/2023/001/BC).

References

1. Jönsson T, Granfeldt Y, Åhrén B, Branell UC, Pålsson G, Hansson A, et al. Beneficial effects of a Paleolithic diet on cardiovascular risk factors in type 2 diabetes: a randomized cross-over pilot study. *Cardiovasc Diabetol* 2009;8:35. doi: 10.1186/1475-2840-8-35.
2. Manheimer EW, van Zuuren EJ, Fedorowicz Z, Pijl H. Paleolithic nutrition for metabolic syndrome: systematic review and meta-analysis. *Am J Clin Nutr* 2015;102:922-32. doi: 10.3945/ajcn.115.113613.
3. Gjermani E, Fiebiger R, Bundalian L, et al. The impact of dietary interventions on cardiometabolic health. *Cardiovasc Diabetol* 2025;24:234. doi: 10.1186/s12933-025-02766-w.
4. de Menezes EVA, Sampaio HAC, Carioca AAF, et al. Influence of Paleolithic diet on anthropometric markers in chronic diseases: systematic review and meta-analysis. *Nutr J* 2019;18:41. doi: 10.1186/s12937-019-0457-z.
5. Fraczek B, Pieta A, Burda A, Mazur-Kurach P, Tyrła F. Paleolithic diet—effect on the health status and performance of athletes? *Nutrients* 2021;13:1019. doi: 10.3390/nu13031019.
6. Jönsson T, Granfeldt Y, Erlanson-Albertsson C, Åhrén B, Lindeberg S. A paleolithic diet is more satiating per calorie than a mediterranean-like diet in individuals with ischemic heart disease. *Nutr Metab (Lond)* 2010;7:85. doi: 10.1186/1743-7075-7-85.
7. Şahin Bayram S. A narrative review of the significance of popular diets in diabetes mellitus management. *Cureus* 2024;16:e61045. doi: 10.7759/cureus.61045.
8. Pieta A, Fraczek B, Wiecek M, Mazur-Kurach P. Impact of Paleo diet on body composition, carbohydrate and fat metabolism of professional handball players. *Nutrients* 2023;15:4155. doi: 10.3390/nu15194155.
9. Jamka M, Kulczyński B, Juruć A, Gramza-Michałowska A, Stokes CS, Walkowiak J. The effect of the Paleolithic diet vs. healthy diets on glucose and insulin homeostasis: a systematic review and meta-analysis of randomized controlled trials. *J Clin Med* 2020;9:296. doi: 10.3390/jcm9020296.
10. Landry MJ, Crimarco A, Gardner CD. Benefits of low carbohydrate diets: a settled question or still controversial? *Curr Obes Rep* 2021;10:409-22. doi: 10.1007/s13679-021-00451-z.
11. Tahreem A, Rakha A, Rabail R, Nazir A, Socol CT, Maerescu CM, Aadil RM. Fad diets: facts and fiction. *Front Nutr* 2022;9:960922. doi:10.3389/fnut.2022.960922.
12. Kumar NK, Merrill JD, Carlson S, German J, Yancy WS Jr. Adherence to low-carbohydrate diets in patients with diabetes: a narrative review. *Diabetes Metab Syndr Obes* 2022;15:477-98. doi: 10.2147/DMSO.S292742.
13. Lennerz BS, Koutnik AP, Azova S, Wolfsdorf JL, Ludwig DS. Carbohydrate restriction for diabetes: rediscovering centuries-old wisdom. *J Clin Invest* 2021;131:e142246. doi: 10.1172/JCI142246.
14. Jing T, Zhang S, Bai M, Chen Z, Gao S, Li S, et al. Effect of dietary approaches on glycemic control in patients with type 2 diabetes: a systematic review with network meta-analysis of randomized trials. *Nutrients* 2023;15:3156. doi: 10.3390/nu15143156.
15. Minari TP, Tácito LHB, Yugar LBT, Ferreira-Melo SE, Manzano CF, Pires AC, et al. Nutritional strategies for the management of type 2 diabetes mellitus: a narrative review. *Nutrients* 2023;15:5096. doi: 10.3390/nu15245096.
16. Otten J, Stomby A, Waling M, Isaksson A, Tellström A, Lundin-Olsson L, et al. Benefits of a Paleolithic diet with and without supervised exercise on fat mass, insulin sensitivity, and glycemic control: a randomized controlled trial in individuals with type 2 diabetes. *Diabetes Metab Res Rev* 2017;33:e2828. doi: 10.1002/dmrr.2828.
17. Klonoff DC. The beneficial effects of a Paleolithic diet on type 2 diabetes and other risk factors for cardiovascular disease. *J Diabetes Sci Technol* 2009;3:1229-32. doi: 10.1177/193229680900300601.
18. Clemente-Suárez VJ, Mielgo-Ayuso J, Martín-Rodríguez A, et al. The burden of carbohydrates in health and disease. *Nutrients* 2022;14:3809. doi: 10.3390/nu14183809.