DO YOU KNOW WHAT Lp(a) IS?

Questions and Answers

By

Rajendra V. Prasad, MD, FRCPC

Ex-Associate Professor of Medicine

\

Have you seen young Indians having heart attacks and dying? Do you know why? If you don't please read below.

Elevated Lipoprotein(a), or Lp(a), is increasingly recognized as a significant cardiovascular risk factor in the Iranian population—especially for premature coronary artery disease (CAD). Here's a synthesis of key findings from recent studies:

IR Lp(a) Elevation in Iranians: What the Data Shows

Independent Risk Factor for Premature CAD

- A study from Rajaie Cardiovascular Center found that Lp(a) levels were significantly elevated in Iranian patients with early-onset CAD, even when traditional risk factors (like hypertension or diabetes) were absent.
- Mean Lp(a) levels in a ected individuals were 2.341 µmol/L, with a P-value < 0.001, confirming statistical significance.

Population-Level Comparison

- Another study compared 117 CAD patients with 103 healthy controls:
- CAD group: Mean Lp(a) = 41 ± 40 mg/dL
- Control group: Mean Lp(a) = 25.5 ± 28 mg/dL
- The di erence was highly significant (P < 0.001).

Risk Stratification Enhancement

- Incorporating Lp(a) into the Framingham Risk Score (FRS) improved coronary heart disease prediction by ~20% Net Reclassification Index (NRI) in a 10-year Iranian cohort study.
- This suggests Lp(a) adds predictive value beyond conventional lipid panels.

What is Lp(a)?:

Lp(a), or lipoprotein(a)—pronounced "L-P-little-a"—is a genetically inherited type of lipoprotein that plays a significant role in cardiovascular health. It's like LDL (the "bad" cholesterol), but with an extra protein called apolipoprotein(a) attached, which gives it some unique and problematic traits.

Genetics:

- Genetically determined: Your Lp(a) level is set mostly by your genes and doesn't change much with diet or lifestyle. Lp(a) is inherited in an autosomal codominant pattern— not recessive, not strictly dominant.

What "Autosomal Codominant" Means

- Autosomal: The gene responsible (LPA) is located on a non-sex chromosome, so both males and females inherit it equally.
- Codominant: You inherit one copy of the LPA gene from each parent, and both copies actively influence your Lp(a) level.
- If one parent has a high-producing allele, you may inherit elevated Lp(a).
- If both parents do, your levels could be even higher.
- The actual Lp(a) concentration depends on the number of Kringle IV type 2 (KIV-2) repeats in each allele—fewer repeats = smaller apo(a) isoform = higher Lp(a) levels.
- Independent risk factor: High Lp(a) levels are linked to increased risk of:
- Heart attack
- Stroke
- Aortic stenosis (narrowing of the heart's aortic valve)
- Pro-inflammatory and pro-thrombo c: It promotes inflamma on and clot forma on, which can accelerate plaque buildup and vessel blockage.

Consanguinity and Lp(a): Theore cal Risk

While no direct studies link consanguineous marriage to increased Lp(a) levels, here's the plausible mechanism:

- In popula ons with high baseline Lp(a) (e.g. South Asians), consanguinity may increase homozygosity for high-producing LPA alleles.

- This could theore cally amplify cardiovascular risk, especially if both parents carry highexpression variants.

Popula on-Level Considera ons

- South India, where consanguineous marriages are more common, also shows higher prevalence of elevated Lp(a) and premature coronary artery disease.
- However, this correla on may be confounded by other gene c and environmental factors, and not solely due to consanguinity.

What are the Ethnic Variations in Lp(a) Levels and Risk?

- African ancestry: Highest median levels, but paradoxically, some protective isoform patterns may reduce CAD risk—though stroke risk remains high.
- South Asians: High Lp(a) levels with small isoforms—especially atherogenic. Strong correlation with premature coronary artery disease.
- Isoform size matters: Smaller isoforms are more dangerous. South Asians tend to have smaller isoforms, while African ancestry groups may have larger, less atherogenic ones.

Among Indians, approximately 25–42% have elevated levels of Lipoprotein(a) [Lp(a)], depending on the threshold used and the population studied.

Breakdown of Lp(a) Elevation in Indians

>30 mg/dl	about 25%	elevated risk begins here
>50 mg/dl	about 28%	strongly associated with premature coronary artery disease
>70 mg/dl	about 21%	high risk category for atheroscleoris
>90 mg/dl	about 26%	very high risk: often multivessel coronary artery disease

At what age can someone have this blood test and who in the family should be screened?

If you have high lipoprotein(a), or Lp(a), it's smart to think about cascade screening—a strategy used for inherited conditions like this one. Since Lp(a) levels are genetically determined and stable from early childhood, here’s who should be considered for screening:

Who in the family should be screened

- First-degree relatives: Parents, siblings, and children. They have a 50% chance of inheriting elevated Lp(a) levels.

- Second-degree relatives: Grandparents, aunts, uncles, nieces, nephews—especially if there's a family history of premature cardiovascular disease.
- Children: Testing can be done as early as age 5, since adult levels are typically reached by then.

Why it matters

- Elevated Lp(a) is an independent risk factor for atherosclerosis, heart attack, stroke, and aortic valve disease—even if LDL and lifestyle factors are well-controlled.
- Early detection allows for risk stratification and proactive management, including more aggressive LDL-lowering strategies or consideration of emerging therapies.

What to do next

- A simple blood test can measure Lp(a), ideally in nmol/L (preferred) or mg/dL.
- Discuss with your healthcare provider about initiating cascade screening for your family. It’s especially important if there’s a history of:
- Premature heart disease (men <55, women <65)
- Familial hypercholesterolemia
- Stroke or aortic valve disease without clear cause

How to treat elevated Lp(a)? Current Management Approach (2025)

While no FDA-approved drugs specifically target Lp(a) yet, clinicians aim to reduce overall cardiovascular risk:

Risk Reduction Strategies

- Aggressive LDL-C lowering:
- Statins: Lower LDL but may not reduce Lp(a); still beneficial for overall risk.
- PCSK9 inhibitors (e.g., Repatha, Praluent): Can lower Lp(a) by ~20–30%.
- Inclisiran (Leqvio): siRNA-based LDL-lowering; modest Lp(a) reduction (~26%).
- Low-dose aspirin: May help reduce clotting risk in select individuals with high Lp(a), though evidence is evolving.

- Lifestyle optimization: While it doesn't lower Lp(a), it supports vascular health:
- Plant-based diet, regular exercise, blood pressure control, and avoiding smoking.

Emerging Therapies in the Pipeline

Several Lp(a)-targeted drugs are in late-stage trials:

Pelacarsan, Olpasiran, Zerlasiran, and Muvalaplin are therapies that target the LPA gene directly, reducing production of apolipoprotein(a)—the unique component of Lp(a).

Treating high lipoprotein(a)—or Lp(a)—is a frontier in cardiovascular medicine. Since Lp(a) is genetically determined and largely unaffected by diet or exercise, the focus is on risk management and emerging therapies.

"My heartfelt thanks to Copilot for being a tireless thought partner in this journey of exploration and optimization."