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Issue

New research shows that a mysterious set of genetic factors put Indians at high risk. Can anything be done?

By Neeraj Mishra And Supriya Bezbaruah



To the outside world, Amar Banerjee, 42, was at the prime of his career and seemingly in good health. Banerjee, a Bhopal-based sales executive, was careful with the way he treated his body—he was a regular at the gym, rarely smoked, went easy on the sweet stuff and avoided late nights. A heart attack was the farthest thing from his mind though a few years earlier, his ageing mother had suffered one.

Then one evening, while returning home, Banerjee felt a sharp pain sear through his left chest and felt his arm turn limp. It was so intense that he almost lost balance and dashed his scooter against the sidewalk. He felt nauseated and knew there was something terribly wrong with him. He was rushed to a local hospital where doctors diagnosed his condition as a myocardial infarct caused by excessive clogging of the arteries in his heart.

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Banerjee was stunned. Given the fact that he led a relatively healthy lifestyle, being diagnosed with a serious heart problem was incomprehensible. But the doctors were not surprised. For them, Banerjee was one more victim of Syndrome X—a condition that predisposes Indians to a whole repertoire of biochemical bullets blasting the heart. Syndrome X is now increasingly seen by experts as the prime culprit for the alarming rise in heart diseases in the country. Ironically the understanding of its potential for mischief came from several recent studies of Indians living in the US. The most important is a recently concluded 10-year study of 4,500 patients by the Coronary Artery Disease Institute (CADI) in Lisle, Illinois, that found the Indian community had much higher levels of a deadly genetic factor called lipoprotein A, or LP(a), than other ethnic groups. It is 10 times deadlier in causing clogged arteries that lead to heart attacks than bad cholesterol such as Low Density Lipoproteins (LDL).

Fresh Findings

Syndrome X makes Indians four times more susceptible to heart attacks than Europeans, Americans, Japanese and Chinese.

It puts Indians under 40 at a tenfold higher risk than others.

Indian women are as vulnerable to the disease as men.

WHO predicts that by 2010 India will have 60 per cent of the world's heart patients.

Spearheaded by LP(a) the extraordinary factors called Cardiac Syndrome X by specialists leave Indians four times more prone to heart disease than Chinese, Japanese, Caucasians and Hispanics. "We're in the midst of a heart disease epidemic," says Professor S.C. Manchanda, head of cardiology at the All India Institute of Medical Sciences (AIIMS), Delhi. "In India, approximately four people die of heart attacks every minute because Indians are genetically predisposed to the disease."

But how exactly and why? Like FBI agents probing abnormal phenomena in the popular TV serial, the medical fraternity is racing to discover the cause and effects of Syndrome X. At the heart of the matter is the heart itself. The fist-sized organ is among the most hard working in the body. As precise as a clock, it pulsates almost every second, pumping 10-15 tonnes of blood a day-enough to flood a basketball court-to keep the body alive. For doing this, the heart muscles

require enormous amounts of energy. Oxygen-drawn from the respiratory system and absorbed by blood that reaches the heart through the blood vessels-is its main fuel. Much like water seeping through a blocked pipe, the blood flow slows down when the arteries are clogged. When large clots reduce blood flow to a trickle, the oxygen-starved heart muscles start dying. The result is a heart attack. Similar blockage in brain arteries causes a stroke. Other organs have more vessels, so the blood/oxygen flow is not throttled.

Every day, the heart and its circulatory system are engaged in a battle of biblical proportions to keep the main highways of blood transportation free from blockage. The cloggers-in-chief are cholesterol-soft, waxy substances produced by the liver. Their daily job is to maintain cell walls, hormones and other tissues. As they piggy-back on proteins in the blood, they are named according to the type of carrier they associate with and can be classified as the good, the bad and the ugly.

First, the bad: excess LDL cholesterol fall along the arterial wayside and create havoc. Accumulated LDL cholesterol then clings to the walls of blood vessels and (HDL)-rush in, modifies its form, damaging and scrapping off the cells lining the vessel. All this activity attracts immune cells which then get trapped. LDL cholesterol, immune cells, vessel-lining cells and other substances jammed together, form a thick, hard, deposit called plaque, which gets thicker with time to clog the arteries. Cheering LDL on in its malevolent ways is a fat called triglyceride (TG), an ugly customer obtained from foods like butter, and present in blood to provide instant energy or stored as body fat for future use. As the arteries watch helplessly, the good cholesterol-High Density Lipoprotein (HDL)-rush in, preventing clogging by

SAMEER KUMAR, 30, *Sales Executive, Bhopal*

While playing cricket recently, Kumar collapsed on the field. In the hospital, doctors told a surprised Kumar that he had suffered a heart attack. An avid sportsman, Kumar did not smoke and was a teetotaler. Doctors see him as a victim of cardiac Syndrome X, a disease that strikes Indians more than it does others.

mopping up the littered cholesterol and shuttling them back to the liver. So plenty of HDL cholesterol and less of LDL cholesterol and TG would be the condition of choice to prevent a heart attack.

Among Indians, it's as if all the worst conditions for heart disease were hand-picked and clubbed together to complicate matters as Syndrome X. It bombards Indians with high levels of LDL, low levels of HDL, high TGs and insensitivity to insulin (a cause of diabetes), to compound their susceptibility to hypertension and "central" obesity.

International studies detected this Indian peculiarity. In 1958, research conducted in Singapore first established that Indians have thicker blood and more of LP(a) than the Chinese. The significance was not well understood, till 1990, when Dr Enas K. Enas, CADI's director studying over 4,500 patients, found that the US-based Indian community displayed similar tendencies that doctors began to pay heed. A subsequent 10-year study conducted by Enas confirmed that one out of four Indian-Americans had high levels of LP(a) as compared to the Japanese, Chinese, Caucasians and Hispanics.

The Real Villain

Recently, a study in Singapore which took blood from the natal chord of 5,000 babies of Indian origin, found extraordinarily high contents of LP(a) present, indicating that genetics, not diet, was the major cause of such abnormal levels of LP(a). "This test belies theories about stress, high cholesterol and other essential Coronary Artery Disease (CAD) indicators, as newborns could not have possibly endured all that. Indians, per se, are at a high risk," says Enas.

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Only now is research exposing just how big a villain LP(a) is. According to Dr D.S. Gambhir, president of the Delhi Cardiological Society, on its own, LP(a) causes arterial hardening and blockage. Enas lists LP(a) as the little-known cousin of the LDL family, 15 times deadlier than total cholesterol in off-loading fatty debris in blood. "Indians are in double jeopardy through nature and nurture-nature has given them LP(a) which, in turn, is being nurtured by unhealthy lifestyles associated with rising affluence and mechanisation," says Enas.

The presence of risk factors along with LP(a) increases the incidence of CAD by five times among Indians as compared to other communities. However, LP(a) alone cannot explain why Indians are at such high risk because as a race, Africans, not Indians, have the highest levels of LP(a) and the lowest rate of heart disease in the world. Part of the reason is that Africans have much lower levels of LDL and TG than Indians do.

What exactly LP(a) does to the blood is unclear, but the process closely resembles a clotting factor that helps heal cuts. Scientists suspect that it tricks blood factors within our vessels into clotting into a thick slush. The LDL-induced plaque, generously scattered along the length of the arteries, encouraged as usual by TG, reduces the flow to excruciatingly low rates. This has the heart muscles gasping for oxygen. Then, insulin, which normally helps by dilating blood vessels, does the opposite in all the confusion-when the lining is damaged, it encourages muscle growth which further narrows the arteries.



ENAS K. ENAS,
Director,
CADI, USA
"Indians face the highest risk. Genetics load the gun, lifestyle pulls the trigger."

Clearing the passage for the blood and oxygen involves fighting enormous odds. Nevertheless, HDL in optimal strength may have been up to it, quickly mopping it all up back to the liver. But Indian genes ensure that HDL levels are below normal. A major heart study of over 5,000 patients in the US in 1996 found that only 14 per cent of Indian-American men and five per cent of Indian-American women had optimal HDL cholesterol levels. It's a triple, sometimes quadruple, whammy. For while Americans and Europeans often suffer from one blocked artery, double or triple artery disease among Indians isn't uncommon. The fat deposits in Indians also extend over a greater area, whereas in the west it is generally in one

region.

As a result, Indians across the globe, even third-generation emigrants, fall like ninepins to cardiac disease-they are at least four times more susceptible to CAD than Europeans, Chinese or Blacks, and this risk increases up to ten times in those younger than 40. That's Syndrome X.

Also, heart disease in India is now the malaise of the young rather than the elderly. Today, one in four heart-related problems in the country occur in a man below 42 years and heart disease is the leading cause of death in urban areas. In comparison, the figure is less than four in 100 for the same age group in the US where deaths due to coronary disease have decreased by 40 per cent. Indian women are also not unscathed. Attests Mumbai-based cardiovascular surgeon Sharad Pandey: "Women between 30-35 years of age, largely considered safe from heart trouble before menopause, are now being afflicted by the disease."



RADHE SHYAM, 35,
Gardener, Thermal Power House,
Faridabad
 He wasn't in the category that doctors would put on the high risk for heart attacks. Yet, on his way home from work one evening, Shyam felt a sharp pain sear through his chest. He thought it was gas but rushed to the hospital. After an examination, doctors recommended bypass surgery.



BOB KIM-FARLEY
India representative,
WHO
"India is now burdened with battling diseases like TB as well as high rates of heart attacks."

In India, CAD and diabetes are frequently locked in a diabolic embrace, and to a certain extent insulin insensitivity of syndrome X provides a clue. It's predicted that in the next 10 years, one of four Indians will suffer from diabetes, and that heart ailments will increase proportionately. Says Naresh Trehan, cardiac surgeon and director, Escorts Heart Institute and Research Centre, Delhi: "The increasing number of undetected diabetes is a major cause of CAD."

A Dysfunctional Profile

Why are Indians prone to Syndrome X? The "Starvation Gene Theory" provides an explanation, says Trehan. India suffered droughts for hundreds of years. Fats and carbohydrates provide energy to the body. So our genes adapted to survive long periods of drought by consuming fats and carbohydrates slowly to make them last longer. Now our bodies get adequate supplies of food, but these genes are still in action as they take a long time to adapt, so our food continues to be metabolised slowly resulting in the dysfunctional biochemical profile that constitutes Syndrome X. Other genes have also been blamed. High levels of the amino acid homocysteine also increases the risk of heart disease by activating LDL and clot formation.

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Not all cardiologists subscribe to the theory of genetic heart disease. Mumbai-based cardiac surgeon Nityanath V. Manke points to stress rather than genetics as being the causative factor. "The proposition that increased LP(a) in the blood causes heart disease doesn't work," says Manke. "That way everyone suffering from hyperlipemia (excessive quantity of fat in the blood) would automatically be a candidate for heart disease which doesn't hold true."



NARESH TREHAN

Director, Escorts Heart Institute

"Syndrome X is related to the Starvation Gene factor in Indians caused by prolonged drought over the years."

However, genes alone don't explain the sudden spurt in heart disease among the young. The answer, in a word, is lifestyle. "Genetics load the gun, lifestyle pulls the trigger," is how Enas describes it. Upendra Kaul, president of the Cardiology Society of India, agrees. "Lifestyle changes due to rapid urbanisation are the precipitating cause of heart disease in India," he says. While over 10 per cent of urban Indians succumb to heart disease, the figure is only 3.5 per cent in rural areas. Emphasises Trehan: "Undetected diabetics, hypertension, a fat-rich diet, heavy smoking, lack of exercise and late detection are all recipes for disaster." The cost of harbouring India's 50 million heart patients is phenomenal—the equivalent of \$150 billion (Rs 6,90,000 crore). "The worst aspect of the disease, apart from the human cost, is that it strikes young people and affects their earnings," says Kaul.

The solution to these sky-rocketing figures? Simply tweaking our lifestyles a little. "CAD can only be prevented and only the well-informed can prevent it," says Dr B.S. Yadav, heart specialist at the Gandhi Medical College,

Bhopal. Declares Manchanda: "Cutting down smoking by 5 per cent can be more effective than setting up 10 specialised hospitals." Early detection also reins in the situation. "Every Indian male over the age of 25 and every female over 35 should be tested," says Enas, "because death may be the first symptom of a heart problem." A recent study of young executives at Escorts showed that at least 25 per cent of those tested showed all the risk factors but were not aware of it.

Other preventives include medication like statins, angiotensin-converting enzymes and, in high-risk individuals, aspirin, which helps ease the blood flow. Ancient methods can also banish this very modern malaise. Yoga, show studies at AIIMS, can reverse arterial blocks, while daily walks help control CAD by increasing levels of HDL, the good cholesterol. The government and agencies like the World Health Organisation (WHO) are also awakening to the problem. "India bears the double burden of epidemics of communicable and non-communicable diseases," says Dr Bob Kim-Farley, WHO's India representative. "On one hand, you have problems like tuberculosis, on the other, cancer and heart diseases."

WHO predicts that India will have 100 million, or 60 per cent of the world's heart patients, by 2010. The scenario is of a nation crippled by heart disease. While doctors tinker with the hows and whys, each individual has the weapons to fight back. Lifestyle choices have never been more important in determining the outcome of a national problem.



NITYANATH V. MANKE
Surgeon, Leelavati Hospital

"Let's not give a finality to these conclusions. There still are many unexplained factors."

-With Natasha Israni in Mumbai