

Hyperinsulinaemia, Diabetes and Coronary Heart Disease in India

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Non-Insulin-Dependent Diabetes Mellitus (NIDDM, Type 2 diabetes) constitutes about 95% of the diabetics seen all over the world, as well as in our country. In contrast to Insulin-Dependent Diabetes Mellitus (IDDM, Type 1 diabetes) where an absolute deficiency of insulin is the major defect, insulin resistance is perhaps the dominant factor in the aetiopathogenesis of NIDDM.

Several facets of NIDDM have particular relevance to Asian Indians. Firstly, it is now well recognised that the overall prevalence of diabetes is very high, not only among migrant Indians but also within the Indian subcontinent [1]. Secondly, NIDDM presents at a younger age and the entity called as maturity-onset diabetes of the youth (MODY) is far more common among Indians than among Europeans [2]. Finally, it is being increasingly recognised that the overall prevalence of coronary artery disease is higher among Indians (especially migrant Indians) compared to Europeans [3].

Recently, the role of hyperinsulinaemia in the pathogenesis of diabetes and also its pivotal role in the pathogenesis of associated syndromes like hypertension, dyslipidaemia, obesity and coronary artery disease (Syndrome X or Reaven's Syndrome) have come into focus [4].

High prevalence of Diabetes and Insulin Resistance in Asian Indians

The prevalence of diabetes is known to be very high in migrant Indians. This has been confirmed by studies done in Singapore, Trinidad and the UK. Recent surveys have shown a marked increase in the prevalence of diabetes even within India.

It is possible that hyperinsulinaemia and insulin resistance could be the underlying mechanisms for high prevalence of diabetes mellitus among Asian Indians. To test this hypothesis, Mohan et al [5] took up a study at the Hammersmith Hospital, London. In this study, serum immunoreactive insulin response to an oral glucose load was compared in matched groups of Asian Indian and European control non-diabetic subjects and NIDDM patients. It was found that basal (fasting) insulin values as well as stimulated values (after an oral glucose load) were significantly higher in Asian Indians both among diabetics and non-diabetics compared to their European counterparts.

Table-1
Plasma Insulin Levels (mU/L) in Asian Indians and Europeans [5]

Basal Insulin	Indians	Europeans	P Value
Non-Diabetics	16.7 ± 3.0	vs 6.9 ± 0.9	0.001
Diabetics	18.0 ± 3.0	vs 11.5 ± 0.9	0.05

Simultaneously, Mohan and colleagues [6] also studied insulin resistance in a group of newly diagnosed NIDDM patients of Asian Indian and European origin using the euglycaemic clamp technique. The results of this study showed that Asian Indian diabetic patients were more insulin resistant than their European counterparts. These studies have subsequently been confirmed by other workers. This suggests that hyperinsulinaemia and insulin resistance may be responsible for high prevalence of diabetes among Indians.

Hyperinsulinaemia : link between obesity and diabetes

The close association between obesity and non-insulin-dependent diabetes mellitus is well established. It is also well known that obesity is associated with increased insulin resistance. The contributing mechanisms resulting in peripheral insulinaemia in obesity are (a) increased insulin secretion, (b) decreased hepatic uptake and (c) decreased peripheral metabolism.

In developing countries like India, the prevalence of NIDDM is very high. This is more striking when we realise that the population of these countries is essentially a non-obese one. Recent studies have drawn attention to the role of central (android) distribution of body fat rather than generalised obesity in the causation of diabetes. Shelgikar et al [7] and others have studied the relationship between body mass index (BMI) and waist-hip ratio and diabetes in the Indian subjects. They found that an increase in waist-hip ratio (central obesity) correlates strongly with the occurrence of diabetes.

Relationship between hyperinsulinaemia related to hypertension

Hypertension contributes significantly to morbidity and mortality in NIDDM patients. About 30-50% of

NIDDM patients have hypertension. Conversely, approximately 50% of hypertensive individuals are estimated to have hyperinsulinaemia. Insulin resistance leads to alteration in energy needs of the cell. This in turn results in increased sensitivity of the vascular smooth muscle to catecholamines. Hyperinsulinism also leads to increased sodium and water retention. Proliferation of arteriolar smooth muscle cells (due to stimulation of growth factors by insulin) is another hypothesis for development of hypertension.

Hyperinsulinaemia and coronary artery disease in Asian Indians

Hyperinsulinaemia may directly produce deleterious changes in metabolic activity of arterial wall cells. Recent experimental evidence suggests that hyperinsulinaemia may be linked with atherosclerotic vascular disease (Insulin-atheroma hypothesis). Hyperinsulinaemia is also associated with lipid abnormalities including increased total cholesterol, VLDL and triglycerides, decreased HDL - cholesterol and alteration in LDL composition and density resulting in more atherogenic particles.

The association of coronary artery disease (CAD) with insulin insensitivity is well known. This is particularly relevant to Asian Indians. Hughes et al [8] studied survivors of an initial myocardial infarction in London and showed that Asian Indians had higher two-hour plasma insulin and C-peptide levels after an oral glucose load compared to Europeans. This confirms the earlier observations that Asian Indians have higher insulin levels compared to Europeans [4].

At least three studies from UK have now confirmed that prevalence of coronary artery disease is several-fold higher among Asian Indians. What is more disturbing is that CAD occurs at a younger age among Indians; the age often ranging from 25-39 years, whereas it rarely occurs below the age of 40 years among Europeans. Moreover, the frequency of triple vessel disease is more common in Asian Indians compared to Europeans. This suggests that the severity of CAD is greater in Asian Indians. It is tempting to speculate that hyperinsulinaemia could be the responsible factor, although much more evidence is needed to confirm this.

Management of Hyperinsulinism

The basic principles of treatment of hyperinsulinaemia are diet, exercise and drugs. A

hypocaloric diet will improve insulin action, especially in overweight subjects. A reduction in fat intake and an increase in fibre-rich foods not only helps to reduce body weight, but also improves the insulin sensitivity.

Physical activity significantly regulates insulin action. Chronic conditioned exercise stimulates glucose transport in the cells, even in the absence of insulin.

Oral hypoglycaemic drugs have been shown to have a beneficial effect on insulin receptor number and action. Sulphonylureas are known to increase receptor numbers at the cell surface. Biguanides significantly enhance the receptor affinity and insulin binding.

In summary, the role of hyperinsulinism needs to be studied further. Detection and correction of hyperinsulinaemia by diet, exercise and drugs may help to bring down the morbidity and mortality associated with the silent killers: diabetes, hypertension and coronary artery disease. This will be a challenge to the physicians in the future.

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