

Lessons from Prevention and Control of Type 2 Diabetes in India for Other Noncommunicable Diseases in South-East Asia Region

Noncommunicable (NCDs) are now a major cause of morbidity and mortality globally. In the South East Asia (SEA) region, just four NCDs namely cardiovascular diseases (CVD), diabetes, chronic respiratory disorders and cancer account for ~8.5 million deaths/year.^[1,2] Type 2 diabetes (T2DM) can be taken as an exemplar of NCDs as its prevalence generally reflects that of other metabolic NCDs like hypertension, obesity and cardiovascular disease. It is also one of the easiest to measure and track among all the NCDs. According to the International Diabetes Federation (IDF), estimates in 2021, the SEA region consisting of 7 countries namely Bangladesh, Bhutan, India, Maldives, Mauritius, Nepal and Sri Lanka, is home to 90.2 million adults with diabetes, of which India alone contributes 74.2 million and this number is expected to increase to 125 million by 2045.^[3] In this review, we will mostly deal with T2DM as a model of NCDs and focus mainly on studies done in India. We do however believe that the lessons learnt from the prevention of T2DM in India will be applicable to other SEA countries. Moreover, at the primary prevention level, if the risk factors for T2DM are controlled, this can lead to prevention of several other NCDs as well.

The prevalence of diabetes is still spiralling upwards in India. Till the 1990's, the prevalence of diabetes was low within India but much higher among migrant Indians living in UK, USA and other countries.^[4] Thus, when the prevalence of diabetes in 1970s was 2% among urban and 1% among rural Indians, migrant Indians already had prevalence rates ranging from 7-12%.^[5,6] However, during the last two to three decades, the prevalence of diabetes in India started increasing rapidly and our recent studies suggest that prevalence rates of diabetes are now 22-24% in metropolitan cities like Chennai and Delhi which are far higher than in migrant Indians in California.^[7,8] However, in India itself, there is considerable heterogeneity and there are wide differences in diabetes prevalence between urban and rural areas. Hence, in order to obtain reliable data on the national and state wise prevalence of diabetes in India, a national study was undertaken.^[9]

The Indian Council of Medical Research, India Diabetes (ICMR-INDIAB) study is the largest epidemiological study done on diabetes in India and covers all the 29 states and 2 union territories of the country and the National Capital Region of Delhi. The study estimated the prevalence of various NCDs such as diabetes, hypertension, dyslipidemia and obesity. While the overall prevalence of diabetes was 7.3%, when we looked at the Gross Domestic Product (GDP) of various states in relation

to prevalence of diabetes, it was seen that the diabetes prevalence was higher in states with higher GDP.^[10] Worryingly, over 50% of people were unaware of their diabetes indicating low awareness about the disease.^[11] In most states, the rate of pre-diabetes exceeded the rate of diabetes, a forewarning that the epidemic is far from over. Thus, it is clear that effective preventive programmes need to be urgently implemented to tackle the diabetes epidemic in this region.

Three things are noteworthy as far as diabetes in India is concerned. T2DM was earlier considered a disease of the rich. Now, at least in urban areas of the more affluent states, people who belongs to lower socioeconomic strata have higher rates of diabetes. Secondly, the prevalence of diabetes is rapidly increasing in rural areas. Thirdly, it has now started affecting young adults and even adolescents. If the poor develop diabetes, they cannot afford to pay for their treatment. In rural areas, where 70% of the population lives it is not only difficult to find specialised diabetes care but the magnitude of the disorder will spin out of control even if the prevalence rates increase slightly. When youngsters get the disorder, the exposure to the disease is much longer and hence, the risk of complications is much higher, placing a huge burden on the individual, the family and the society.

Why the Epidemic of T2DM in South Asians?

It is being increasingly recognised that the so called 'South Asian Phenotype' contributes to T2DM and other NCDs in south Asians. This phenotype is characterised by increased abdominal obesity and ectopic fat, insulin resistance, low HDL cholesterol, higher triglycerides, low adiponectin levels and a faster decline in pancreatic beta cell function which results in a rapid conversion of prediabetes to diabetes.^[12-20]

One question which often comes up, is whether epidemic of diabetes, is due to genetic factors or is it due to environmental factors?. Over 400 gene variants have been identified with T2DM. Our Genome Wide Association Studies (GWAS) have identified novel genes associated with T2DM in South Asians.^[21-23] However, the relative contribution of genes is quite small, as the prevalence of diabetes rose almost 10 fold in 50 years, from 1970's to 2020's. Obviously genes don't change that rapidly, although, admittedly, epigenetic changes could have occurred. Thus, it is clear that environmental factors contribute far more to the epidemic of diabetes.

Three main environmental factors contribute to the epidemic of T2DM and other metabolic NCDs in the SEA

region; (i) Excess calories, especially high intake of refined carbohydrates (and possibly fat) (ii) physical inactivity and (iii) Urbanization, probably contributing through air pollution and other mechanisms.

Do Excess Carbohydrates Contribute to T2DM Risk in South East Asia Region?

Rapid economic growth in India and the SEA region has resulted in nutritional transition contributing to excess calories mainly from refined carbohydrates like polished white rice or refined wheat both in rural and urban populations which leads to a high dietary glycemic load.^[24,25] We first showed that consumption of white rice was linked to risk of T2DM in a cross sectional study.^[26] Later, in the Prospective Urban Rural Epidemiology (PURE) Study, a longitudinal study of 132,373 participants aged 35–70 years from 21 countries, we showed that excess polished white rice intake was linked to new onset (i.e., incident) Type II DM and that the risk was higher in South Asia which had the highest intake of white rice.^[27] We also showed that a high glycemic index in the diet was associated with increased mortality.^[28] A randomized control study showed that replacing white rice with brown rice could improve the 24 hour blood glucose and insulin levels.^[29]

It's not just the 'quantity' of the carbohydrates but its 'quality' also which is important. Thus, if the 'bad carbs' like highly polished white rice, refined wheat, white bread and refined flour are replaced with whole grains like brown rice, whole wheat, multi-grain bread and less refined flour, this could substantially reduce the glycemic index and the glycemic load of the diet and thereby help to reduce the burden due to metabolic NCDs like T2DM.

Decreased physical activity is another driver of the diabetes epidemic.^[30] Physical inactivity commonly contributes to energy imbalance and leads to increase in body fat, systemic inflammation, and insulin resistance. These increase the risk for T2DM and CVD.^[31] Conversely, there is reduced risk for NCDs associated with increased physical activity. There is data to suggest that South Asians require greater levels of physical activity to obtain similar cardiometabolic benefits as White Caucasian.^[32]

The Indian Diabetes Prevention Program (IDPP-1) was the first primary prevention of diabetes trial conducted in India.^[33] This study showed that lifestyle modification (LSM) by increasing physical activity and healthier diet could effectively prevent T2DM in Indians. We recently published the results of a large randomized control trial called the 'Diabetes Community Lifestyle Improvement Program (DCLIP)' in people with prediabetes. We found that there was a reduction of incidence of diabetes by 32% in those with impaired glucose tolerance.^[34] However, in those with isolated fasting glycemia (IFG), we could only prevent progression

to T2DM in 12%. Hence more studies are needed on the prevention of progression of IFG to T2DM.

How Much Reduction in Carbohydrate would be needed to Prevent T2DM at a Population Level?

Using the dietary data of individuals in the ICMR-INDIAB study, with normal glucose tolerance, prediabetes and diabetes, macronutrient recommendations were formulated using a constrained quadratic programming problem (QPP) to compute the optimal macronutrient compositions that would help to prevent diabetes or to achieve remission of diabetes. If the carbohydrate content of the diet which currently constitutes 60-70% of calories, could be reduced between 49 – 54% and the protein increased to 19 – 20% and the fat kept at 21 – 26% (mostly coming from healthy fats) both prevention of T2DM as well as its remission could be achieved.^[35] A recent editorial supported this concept while pointing out the need for performing RCTs to prove the hypothesis.^[36]

Thus, improving diet and increasing physical activity stand out as the 'low hanging fruits' which can help in the prevention and control of NCDs like T2DM. Mozaffarian^[37] has shown that an ideal diet would comprise of increased intake of fruits, vegetables, whole grains, fish, dairy and vegetable oils and reduced intake of refined grains, processed/unprocessed meats and sugar-sweetened beverages. The intake of green leafy vegetables and fruits remain low in India and SEA. If subsidies can be given to farmers in the region to make green leafy (non starchy) vegetables and fruits, more available, accessible and affordable, this could help to make diets in India and SEA region, healthier.

Role of Low-Birth Weight

Barker^[38] showed that low birth weight was a risk factor for diabetes in Europeans born in the first half of twentieth century.^[39] These findings were replicated in many other countries. Studies in India also supported a role for intrauterine undernutrition coupled with post-natal 'overnutrition', in the aetiology of T2DM.^[40] This led to the 'thin fat Indian' phenotype which predisposes to metabolic NCDs like T2DM.^[19] Obviously improving maternal health and preventing small, low birth weight babies would be an important public health policy to adopt to prevent NCDs.

What about Environmental Pollutants?

Exposure to *particulate matter 2.5* (PM_{2.5}) pollution was recently found to be the third leading risk factor globally for T2DM related deaths and disability after high blood sugar and excessive body weight.^[41] Globally, such exposure contributed to an estimated 2.76 lakh deaths and 15.2 million life years lost to disability, in 2017. This burden was highest in India, where it accounted for 55,000 deaths and 2.7 million life years lost, according to

the report by Health Effects Institute (HEI) and Institute of Health Metrics and Evaluation's Global Burden of Disease project.^[42]

PM_{2.5} particles are endocrine disruptors. They can affect insulin secretion and insulin sensitivity. They can also damage the beta cells in the pancreas that produces insulin. The exact pathways are not known yet, but increasingly, research is showing a connection between air pollution and T2DM risk. Obviously, this offers yet another possibility for preventing T2DM by reducing air pollution.

In conclusion, a judicious combination of a healthy diet with about 40 – 50% carbohydrates, around 20% protein (especially from plant proteins) and the rest from healthy fats like monosaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) along with adequate physical activity could help to stem the tide of the rising epidemics of NCDs in India and SEA region with special reference to T2DM. Improving maternal nutrition and reducing air pollution could be other priorities to achieve the above goals. A multisectoral collaboration would however be needed, not only between several Governmental departments and Ministries, but also with the civil society and non-governmental agencies. The time to act is NOW!

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