

Diabetes in Asia – From Understanding to Action

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In the present pandemic of diabetes and obesity, 60% of the affected population will come from Asia.¹ Between India and China, these two most populous nations will contribute more than 100 million to the world's population of people with diabetes, many of whom remain undiagnosed, untreated or suboptimally managed.^{2,3} Adding to this disease burden is the predominant increase in disease prevalence in the young-to-middle aged groups, with its implications for premature mortality, quality of life and societal productivity.^{1,4,5} This rising trend of early-onset chronic disease is further fuelled by the increasing prevalence of obesity and the metabolic syndrome in Asian children and adolescents, many of whom already harbour subclinical atherosclerosis and albuminuria, a powerful predictor for cardio-renal complications.⁶⁻⁸

In Asian populations undergoing epidemiological transition, the prevalence of diabetes has increased between 2-fold and 5-fold in the last 2 decades, compared with 1.5 fold in western countries.⁹ For the same body mass index (BMI) or waist circumference, Asian subjects tend to accumulate more body fat than European whites ("Caucasians") and to develop cardiovascular risk factors at considerably lower threshold values of these anthropometric indexes.¹⁰⁻¹² Depending on the definitions used, 10% to 25% of Asian populations have metabolic syndrome,^{13,14} which carries prognostic significance and predicts diabetes as well as cardiovascular and all cause mortality.^{15,16}

In the early 1990s, prospective studies in American Japanese people confirmed the dual impacts of visceral fat and inadequate pancreatic beta-cell response to overcome obesity-associated insulin resistance, on the future risk of diabetes.¹⁷ In the Shanghai Diabetes Survey, over 90% of subjects with impaired glucose regulation had impaired glucose tolerance with or without impaired fasting glycaemia (IFG). The latter was associated with a 15- to 27-fold increased risk of diabetes compared with a 9-fold increase in subjects with isolated IFG.¹⁸

The replication of risk association of type 2 diabetes with genetic variants of TCF7L2, SLC30A8, HHEX, CDKAL1,

CDKN2A/B, IGF2BP2 and FTO in Korean, Chinese, and Japanese populations¹⁹⁻²² reaffirms the importance of beta-cell insufficiency as an important factor in disease manifestation in Asian populations. However, due to inter-ethnic differences in allele frequency or presence of other variants within the same gene, there were major differences in the population attributable risks conferred by these genetic variants between Asian and white European populations, thus emphasising the need to conduct Asian-relevant genetic studies.

Adding to this complexity is the considerable phenotypic and genotypic heterogeneity, especially in young Asian patients, who have a lower prevalence of classical autoimmune type 1 diabetes than their white European counterparts especially in those with young onset of disease and lean body mass.²³ Apart from genes for the maturity onset diabetes of the youth (MODY), genetic variants of the mitochondrial proteins, amylin, and transcription factors, many of which are related to beta-cell structure and function, have also been reported in Japanese, Korean and Chinese populations,²⁴⁻²⁷ while a substantial proportion of diabetic subjects or those at risk exhibit features of early-onset metabolic syndrome.^{28,29}

Apart from rapid changes from a lifestyle typified by energy scarcity to one of energy abundance, some factors highly prevalent in Asia, including low socioeconomic status,³⁰ low grade chronic infection such as those due to hepatitis B virus,^{31,32} and low birth weight³³ may also contribute to the rapid rise in prevalence of diabetes and associated complications in this region. Also, differences in ethnicity, cultures, coexisting diseases, and access to care may explain differences in disease progression and susceptibility to complications between the Asian and White European populations. Several international surveys have confirmed the lower prevalence of coronary heart disease (CHD) (except for South Asians) and the higher prevalence of stroke and kidney disease in Asian than in their White European counterparts.^{9,34,35}

While the low prevalence of hypercholesterolaemia in Asian populations³⁶ may contribute to the low prevalence

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of CHD, the early onset of type 2 diabetes and a long period of undiagnosed or untreated disease² may in part explain the high prevalence of albuminuria, reported to be about 60%,³⁷ and of diabetic kidney disease in Asian populations.³⁸ Importantly, with the onset of diabetic kidney disease, there is further perturbation of the metabolic milieu, including anaemia, vascular calcification, inflammation, oxidative stress and dyslipidemia, all of which substantially multiply the risk of cardiovascular diseases in these subjects.³⁹

Despite the intertwining challenges of diabetes, metabolic syndrome and cardio-renal complications, some prospective studies have confirmed the validity of using simple questionnaire and clinical measurements such as age, sex, family history of diabetes, BMI, waist circumference, and history of hypertension to identify subjects at high risk for diabetes in Asia.⁴⁰

Furthermore, in the last two decades, exemplary prevention programs including lifestyle modification,⁴¹⁻⁴⁴ and disease management programmes⁴⁵⁻⁴⁸ with particular emphasis on early intervention, aggressive glycaemic control, global risk factor management, periodic monitoring, and attainment of treatment targets using an evidence-based and multidisciplinary approach have been initiated in Asia. The marked benefits of these intensive treatment, care and education programs, which reduce the risk of diabetes and associated complications by 30% to 70%, have also been confirmed in White European populations.^{49,50}

During the last two decades, lessons learnt from Asian populations living in societies at different stages of socioeconomic development have provided important insights into the complexity of the pathogenesis of diabetes, involving genetic, perinatal, environmental, socio-economic and lifestyle factors.

Whereas ongoing research is needed to define the causal natures of these complex associations to better diagnose and classify diabetes for interventional studies, there are sufficient data to support the use of a combined strategy consisting of early screening, risk stratification, treatment to targets, and patient empowerment to reduce the impact of these growing disease burdens. To this end, the Japanese Government has recently embarked upon a nation-wide diabetes and obesity prevention programme⁵¹ which adds to the growing list of diabetes care and prevention programs within the region.

The diversity in ethnicity, socio-economic, technological and political developments in Asia has provided ample opportunities for countries within the region to learn and collaborate in a common search for knowledge of particular relevance to people living in this region, who are undergoing phenomenal lifestyle and socioeconomical changes. In this

era of globalisation, Asia has also provided many opportunities for inter-sectoral and interdisciplinary partnerships including governments, professional bodies, industries and interest groups to join forces in a common pursuit of solutions to curb the current pandemic. The solutions found will be relevant to many more developing countries undergoing similar epidemiological transition and health care evolution.

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