Why does visceral adiposity not explain higher type 2 diabetes prevalence in Asian Indians?

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According to the International Diabetes Federation, 60% of all people with type 2 diabetes live in Asia. Indeed, India and China alone contribute over 40% of the world's type 2 diabetes population. In *The Lancet Diabetes & Endocrinology*, Theresia Mina and colleagues report on a study from Singapore using dual-energy x-ray absorptiometry to understand the link between adiposity and metabolic health in people belonging to three ethnicities in Singapore: Chinese, Malay, and Indian.[1] Their hypothesis was that visceral adiposity might elucidate differences in prevalence of cardiometabolic risk factors, particularly type 2 diabetes, across these ethnicities. Using a population cohort of 9067 individuals of whom 68·6% were Chinese, 12·9% Malay, and 18·5% Indian, they report that obesity and type 2 diabetes were 3–4 times more common in Malay and Indian participants compared with Chinese participants. While visceral adiposity was an independent risk factor for metabolic diseases and visceral fat mass index did point to differences in triglycerides and blood pressure, it did not explain the higher glucose levels, reduced insulin sensitivity (greater insulin resistance), or increased risk of type 2 diabetes, particularly among Indians. These findings point to additional mechanisms contributing to the higher susceptibility of Indians to type 2 diabetes. One might argue that part of these findings might be due to the slight differences in sex distribution within the ethnicities studied: among the cohort of 6807 participants not on treatment for type 2 diabetes, hypercholesterolaemia, or hypertension for whom sex-by-ethnicity data are provided, females comprised 63·2% of Chinese and 65·9% of Malay participants, but only 52·9% of Indian participants.

The findings of Mina and colleagues are important for several reasons. Firstly, they confirm findings from earlier studies from Singapore[2] by showing that the prevalence of type 2 diabetes was highest in those of Indian ancestry, followed by Malay and Chinese. Secondly, it is of interest that Indians had the highest insulin resistance at all ages as shown by the homeostatic model assessment for insulin resistance values. Thirdly, the authors estimate that to achieve the insulin sensitivity equivalent to that seen in Chinese participants with mean BMIs of 22·7 kg/m² (females) and 24·1 kg/m² (males), Malay participants would need to have mean BMIs of 23·5 kg/m² (females) and 22·3 kg/m² (males) and Indian participants 19·9 kg/m² and 18·7 kg/m², respectively.

A surprising finding from the study was that the Indians also had the highest insulin secretory responses as shown by the homeostatic model assessment for β-cell function values. This finding is in contrast to recent studies which have shown that Asian Indians with type 2 diabetes have low insulin secretion. Indeed, in a study comparing two groups, Pima Indians (Native Americans) and Asian Indians, both of whom have very high prevalence rates of type 2 diabetes, the Pima Indians were characterised by marked obesity and severe insulin resistance, whereas the Asian Indians (living in Chennai, India) were leaner and had marked insulin deficiency.[3] The differences observed in the study by Mina and colleagues with respect to higher insulin responses in Indians might be related to the stage of the natural history of type 2 diabetes. In early studies done in the UK, we showed higher insulin responses and greater insulin resistance in Indians compared with White Europeans,[4] and this finding was later confirmed by several studies. This phenomenon was also demonstrated in newborn Indian babies, leading to the concept of the "thin-fat" Indian with hyperinsulinaemia and excess adiposity.[5] It is likely that in Indians, following an initial stage of hyperinsulinaemia, there is a rapid decline in β-cell function, resulting in severe insulin secretory defect.[6,7]

There has been a debate in the past about the relative importance of visceral versus subcutaneous adiposity in cardiometabolic risk, including type 2 diabetes, in south Asians. However, a systematic review and meta-analysis comparing liver, visceral, and subcutaneous fat in south Asians and White Europeans, concluded that it is the liver fat which is the predominant defect in south Asians.[8] Unfortunately, liver fat was not reported by Mina and colleagues in their study.

Given that visceral adiposity could not explain the higher prevalence of type 2 diabetes in Indians, what other factors might be responsible? A recent study by

McLaren and colleagues[9] provides some insight into this question. In response to overfeeding and 5–7% gain in bodyweight, south Asians had a smaller increase in lean mass than Europeans. Moreover, the south Asians had fewer small adipocytes, which led to decreased "metabolic buffering" of the fat, leading to increased ectopic fat, especially in the liver. The expression of *SREBF1* also differed between south Asians and White Europeans. These differences might explain why visceral adiposity alone did not explain differences in type 2 diabetes prevalence between south Asians and White Europeans. Furthermore, Mina and colleagues acknowledge in their limitations that they did not adjust their analyses for lifestyle factors such as diet and physical activity levels. We have shown that excess white rice (carbohydrate) intake is an important contributor to type 2 diabetes in south Asians.[10] Future studies could look into the role of lifestyle factors including diet and physical activity, psychosocial, hormonal, and metabolic factors, the role of liver fat, as well as genomic and other omic analyses to explain differences in prevalence rates of type 2 diabetes within Asian ethnicities.

We declare no competing interests.

*Viswanathan Mohan, Ranjit Mohan Anjana
drmohans@diabetes.ind.in
Madras Diabetes Research Foundation & Dr. Mohan's Diabetes Specialities Centre, Chennai 600086, India

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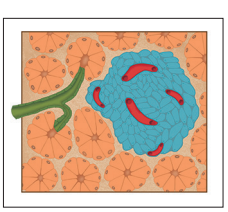
Islet transplantation in kidney transplant recipients with type 1 diabetes

Randomised controlled trials in which islets are transplanted into the portal vein of patients with type 1 diabetes with problematic glycaemic control reported the superiority of islet transplantation for glycaemic control and resolution of hypoglycaemia where intensive insulin treatment had failed.[1]

Results from the kidney alone versus islet-after-kidney (KAIAK) study[2] indicate improved long-term patient survival outcomes in people with type 1 diabetes receiving both kidney and islet-after-kidney (IAK) transplantation versus kidney alone transplants, expanding the indication for IAK transplantation further to complex cases of people living with type 1 diabetes.

This pivotal study, conducted in France between 2000 and 2017, identified 2391 kidney transplant recipients within a nationwide comprehensive registry, of whom 47 also received islet transplantation, with a follow-up period up to 15 years. The study used a population-based target trial emulation approach. By using a 1:2 matching method based on time-dependent propensity scores and taking into consideration various confounding factors, Mehdi Maanaoui and colleagues[2] ensured comparability between patients who received IAK transplantation (≤3 sequential islet infusions in 6 months; n=40) and those treated with kidney alone transplantation (n=80).

Benefits of IAK versus kidney alone transplantation were demonstrated on patient-graft survival: the primary composite outcome measure defined by death, kidney re-transplantation, or return to dialysis. IAK transplantation was associated with a reduction in patient-graft failure (hazard ratio [HR] 0·44, 95% CI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