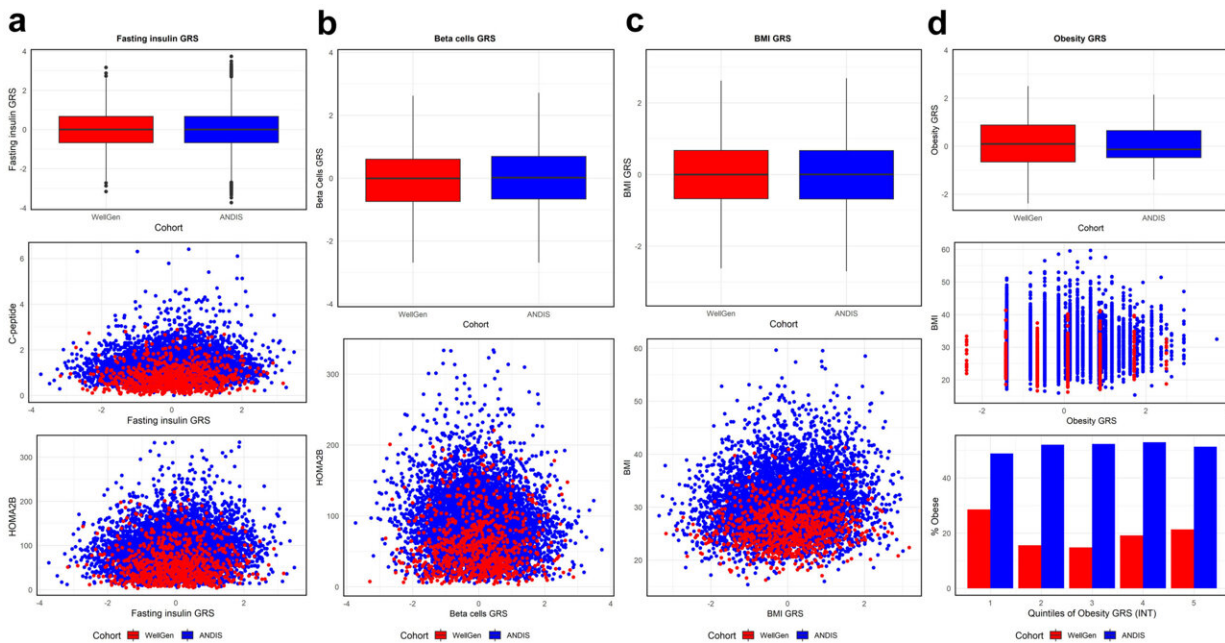# Swedish research about different forms of type 2 diabetes is relevant for Indian people

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Box and whisker plots show distributions of genetic risk scores (GRSs) for fasting insulin (a), beta-cells (b), BMI (c) and obesity (d) in WellGen (India) and ANDIS (Sweden) studies; and scatterplots of related phenotypes for the two populations. WellGen is shown in red and ANDIS in blue. For obesity GRS, proportion of patients with diabetes who are obese (BMI > 30 kg/m^2) are shown in quintiles of GRS. For the same value of GRS, WellGen patients have a lower C-peptide, homeostatic model assessment for beta cell function (HOMA2B), BMI and obesity prevalence compared to ANDIS patients. Credit: *The Lancet Regional Health - Southeast Asia* (2023). DOI: 10.1016/j.lansea.2023.100182

Researchers at Lund University have shown that diabetes can be divided into five subgroups, and that there are genetic differences between the four subgroups relating to type 2 diabetes. A research collaboration between Sweden and India now highlights similarities and differences between patient groups in India and Europe. The knowledge can be used to improve the treatment of the disease in India, where type 2 diabetes represents a growing disease burden.

"The study highlights genetic similarities and differences between different forms of type 2 diabetes in India and Europe. We see this article as an exciting new step towards a better understanding of the development of type 2 diabetes in India," says Rashmi Prasad, associate professor in genomics, diabetes, and endocrinology at Lund University.

Rashmi Prasad is one of the researchers behind an acclaimed study from 2018 that showed that diabetes can be divided into five subgroups based on how the disease develops. In 2021, she and her colleagues at Lu contributed to a new study in *Nature Genetics* that demonstrated that there are genetic differences between the four forms of type 2 diabetes in Sweden.

The new study, published in *The Lancet Regional Health—Southeast Asia,* confirms that the classification system is applicable on a cohort in western India. The results are based on clinical data from 2217 patients and genome-wide associations studies (GWAS) and a genetic risk score analysis (GRS) on 821 people with type 2 diabetes from a study in western India.

"The characteristics of all the subgroups reflected those seen in European people with diabetes. We could also confirm our previous findings that have shown that a certain form of type 2 diabetes that is characterized by relatively low BMI is the most common form of the disease in India," says Rashmi Prasad.

Early life undernutrition

The subgroup in question is called SIDD and this is a form of type 2 diabetes that is also characterized by early onset, low insulin secretion, and poor metabolic control. Of all the participants with type 2 diabetes in the Indian study, 47 percent were classified as belonging to the SIDD group. Previous studies on populations in Sweden have shown that MARD, which is characterized by late onset, is the most common form of diabetes among Swedish people.

"Early life undernutrition in Indians may be a major contribution to early onset of type 2 diabetes, and this may be why we see this difference in the distribution of patients between Sweden and India. The knowledge may be used to prevent the disease in India, which has the second highest number of diabetes worldwide after China. Our findings suggests that efforts to prevent malnutrition in Indians may also prevent type 2 diabetes," says Rashmi Prasad.

Vitamin B12 deficiency

The second largest group in India was MOD, a group which is characterized by obesity, early onset, and a relatively mild disease progression. The Indian group of people in the MOD group were associated with genetic variants for vitamin B12 deficiency, and this was not seen in the Swedish group of people in the MOD group. Vitamin B12 is obtained from animal foods, such as meat and dairy products. B12 deficiency is common in Indian people and is associated with vegetarian food habits.

"It's an interesting example of genetic differences between the Indian and Swedish groups in our study. This finding suggests that the causes of the disease differ between the two populations. Vitamin B12 deficiency may be a factor that drives the disease in the Indian MOD group," says

Rashmi Prasad, who is originally from India.

Rashmi Prasad has led the team of researchers together with professor Chittaranjan S Yajnik at King Edward Memorial (KEM) Hospital and Research Centre in Pune, India. The research exchange was supported by the Swedish Research Council and the Department of Science and Technology (DST) in India. The team would now like to carry out large-scale studies to unravel the characteristics of type 2 diabetes in India.

"Since ancient times physicians have experienced the heterogeneity of diabetes, and our systematic classification may help individualize the treatment and improve outcomes. Type 2 diabetes is a rapidly growing disease burden in India, and many Indians are being diagnosed at a younger age than before. Research like ours will help tackle the causes of the disease and is a step towards prevention," says Chittaranjan S Yajnik, who is a medical doctor and director of the diabetes unit at KEM Hospital.

The five subgroups:

SAID (severe autoimmune diabetes)

SAID includes patients traditionally referred to as patients with type 1 diabetes and latent autoimmune diabetes in adults (LADA). SAID is defined by the presence of GAD autoantibodies and characterized by early onset, poor metabolic control, and low insulin secretion.

SIDD (severe insulin-deficient diabetes)

SIDD is characterized by early onset, low insulin secretion, relatively low BMI, and poor metabolic control. Patients with SIDD also have an increased risk of developing eye retinopathy and neuropathy, which constitutes retinal and nerve damage respectively. In India, diabetic

kidney disease and retinopathy were more prevalent in SIDD compared to Europe.

SIRD (severe insulin-resistant diabetes)

SIRD is characterized by late onset, obesity, insulin resistance and high risk of non-alcoholic fatty liver disease and diabetic kidney disease.

MOD (mild obesity-related diabetes)

MOD is characterized by early onset and obesity and is a relatively mild disease in terms of progression of hyperglycemia and complications. In India, MOD had a higher prevalence of neuropathy compared to Europe.

MARD (mild age-related diabetes)

MARD is characterized by late onset diabetes and relatively good metabolic control.

More information: Chittaranjan S. Yajnik et al, Polygenic scores of diabetes-related traits in subgroups of type 2 diabetes in India: a cohort study, *The Lancet Regional Health—Southeast Asia* (2023). DOI: 10.1016/j.lansea.2023.100182

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