Is Diabetes a cluster of 5 diseases or 2?

Diabetes is presently classified into two main types, Type 1 and Type 2 diabetes. But according to a new study, diabetes can be separated into 5 different types, rather than just Type 1 and Type 2.

Increasing rates of diabetes across the globe is a major concern since ages despite some of the major advances in the field of disease management.

Evidence suggests that early treatment is crucial for prevention of life-shortening complications because target tissues seem to remember poor metabolic control decades later (so-called as the *metabolic memory*).

Existing treatment strategies have been unable to stop the progressive course of the disease and prevent development of chronic diabetic complications. One explanation for these shortcomings can be the diagnosis of diabetes is based on measurement of only one metabolite, glucose, but the disease is heterogeneous with regard to clinical presentation and progression.

The Current Classification

Type 1 diabetes is an autoimmune disease. It is usually diagnosed in childhood and is caused by the body's immune system wrongly attacking & destroying pancreatic cells that make insulin. Without insulin, the body is unable to regulate blood sugar levels.

Type 2 diabetes, most common in people with a prevalence of 85% and 90%. In T2DM the body does not produce enough insulin, or the available insulin does not work properly. It is generally considered a 'lifestyle' disease, as excessive body fat can disrupt the workings of insulin.

A third subgroup, Latent Autoimmune Diabetes in Adults (LADA; affecting <10% of people with diabetes), defined by the presence of Glutamic Acid Decarboxylase Antibodies (GADA), is phenotypically similar to T2DM at diagnosis, but becomes increasingly similar to T1DM over time.

Thus, T1DM and T2DM are very different conditions, but we don’t yet know enough about the subtypes that could exist within them. A refined classification could provide a powerful tool to identify at diagnosis those patients who are at greatest risk of complications and may enable an individualized treatment regimen.
The scientists from Lund University Diabetes Centre and Skåne University Hospital in Malmö, Sweden, and the Institute for Molecular Medicine, Helsinki, Finland, analyzed 5 studies involving 14,775 adults from Sweden and Finland who had recently been diagnosed with diabetes.

They analyzed key measurements of the disease, as well as blood composition and genetic features.

They used 5 diagnostic yardsticks to accurately predict changes in A1C scores over time in both people with T1DM and T2DM as follows:

- Age of onset
- Body mass index (BMI)
- A1C score
- Level of insulin secretion
- Insulin resistance

Refined Classification

5 Clusters

1. Severe Autoimmune Diabetes (SAID)
2. Severe Insulin Deficient Diabetes (SIDD)
3. Severe Insulin Resistance Diabetes (SIRD)
4. Mild Obesity related Diabetes (MOD)
5. Mild Age Related Diabetes (MARD)
They distinguished three severe (Cluster 1, 2 & 3) and two mild (Cluster 4 & 5) forms of disease.

Cluster 1 corresponded to T1DM and the other 4 were subtypes of T2DM.

**Cluster 1 (SAID): Typical Type 1 diabetes from autoimmune reactions**
This is a severe autoimmune form of diabetes close to T1DM affecting around 6% of participants.

**Cluster 2 (SIDD): Beta cell impairment caused by something other than autoimmune reaction**
This consists of relatively young, insulin-deficient individuals with high blood sugar levels, faulty insulin secretion and moderate insulin resistance. Affecting around 18% of individuals, they had the highest level of eye damage.

**Cluster 3 (SIRD): Most insulin-resistance and highest risk of kidney disease**
Characterized by obesity and severe insulin resistance, individuals in this group accounted for ~15% of participants and had the highest incidence of kidney damage.

**Cluster 4 (MOD): The most obese**
Comprises around 21% of cases, who are obese individuals who are not insulin resistant but develop mild diabetes at a relatively young age.

**Cluster 5 (MARD): Diabetes that seems to come as a product of aging**
Mild diabetes among mostly older patients, accounting for ~40% of cases.
**Disease Progression**

- Clusters 1 and 2 had substantially higher HbA1c at diagnosis than the other clusters
- **Ketoacidosis** at diagnosis was most frequent in cluster 1 and cluster 2
- HbA1c was the strongest predictor of ketoacidosis at diagnosis
- Cluster 3 had the highest prevalence of **non alcoholic fatty liver disease (NAFLD)**

**Treatment**

- At registration, **Insulin** had been prescribed to 42% patients in cluster 1, 29% in cluster 2, but to < 4% of patients in clusters 3 to 5
- The proportion of patients on **Metformin** was highest in cluster 2 and lowest in cluster 1, but was also low in cluster 3, which would be expected to benefit the most from **Metformin. (This shows that traditional classification is unable to tailor treatment to the underlying pathogenic defects)**
- Patients in cluster 2 had the shortest time to second oral diabetes treatment and the longest time to reach the treatment goal

**Development of Diabetic Complications**

- **Cluster 3** had the highest risk of developing **chronic kidney disease**
- Early signs of **diabetic retinopathy** were more common in **cluster 2** than in the other clusters
Future Tailored Treatments

- The study reported that many patients were not receiving appropriate treatment.
- It suggests that a more individual approach to the disease could be beneficial.
- These subtypes classification will help in personalized treatments and potentially reduce the risk of diabetes-related complications in the future.
- Nevertheless, till the time it is evaluated in varied patient population and find suitable place in the guidelines, this discovery would be a first step towards individualized tailored treatments for the management of diabetes.


“The best way to predict your FUTURE is to CREATE it.”
-Abram Lincoln

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