

New Perspective on Glucose Metabolism Biomarkers

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The increasing number of diabetes patients is a global matter of urgency. To prevent its onset, early detection of impaired glucose tolerance (IGT) and lifestyle changes are essential. However, early detection of IGT through fasting blood sampling is very challenging; therefore, there is a need to establish markers that can identify IGT and high-risk groups for type 2 diabetes mellitus (T2DM) early using blood samples. The following are the most common biomarkers: blood glucose, hemoglobin A1c, and glycoalbumin. Hemoglobin A1c, in particular, is a valuable diagnostic and prognostic marker of glycemic control in patients with diabetes, as it has been validated in clinical trials to correlate with diabetes-related complications¹⁾⁻³⁾. HbA1c is useful for measuring glycemic control over the preceding three months, with particular emphasis on the preceding 30 days⁴⁾. However, there are conditions that can affect the reliability of HbA1c measurement, such as chronic kidney disease, anemia, and hemoglobinopathies. This study by Shinohara and colleagues is the first to analyze whether serum ferritin levels can serve as a marker for the early detection of IGT or diabetes. In humans, hemoglobin in red blood cells contains 70% of the body's iron⁵⁾. Serum ferritin is widely used as an indicator of body iron stores in clinical medicine⁶⁾. Research has shown a relationship between increased serum ferritin levels and diabetes^{7,8)}. Here, they analyzed the clinical significance of serum ferritin levels using oral glucose tolerance test (OGTT) data in young Japanese individuals with normal glucose tolerance. Among 233 men, ferritin showed a positive correlation with age, HOMA- β , LDL-C, non-HDL-C, hemoglobin, platelet count, and 120-minute post-load plasma glucose and insulin. Multivariate analysis revealed that fasting plasma glucose, ferritin, and non-HDL-C are independent predictors of 120-minute post-load plasma glucose in young men.

Among 149 women, ferritin exhibited a positive correlation with hemoglobin and C-reactive protein (CRP), and a negative correlation with HbA1c and HDL-C. Additionally, an interesting finding was that men with higher ferritin levels showed increased glucose levels at 60 and 120 minutes and increased insulin levels at 120 minutes compared with men who had lower ferritin levels. Women with higher ferritin levels showed lower HDL-C but higher hemoglobin than those with lower ferritin levels. These results suggest that serum ferritin levels and non-HDL-C can be used to independently predict prolonged glucose elevation on OGTT in healthy young Japanese men. This study has several limitations, such as its cross-sectional nature, which provides only indirect evidence of an increased risk for the development of T2DM. To verify these findings, further large-scale prospective studies and exploration of the underlying mechanisms are needed.

Reference

- 1) Holman RR, Paul SK, Bethel MA, et al. 10-Year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med* 2008; 359 (15): 1577-89. Epub 2008 Sep 10.
- 2) Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000; 321 (7258): 405-12.
- 3) Nathan DM; DCCT/EDIC Research Group. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study at 30 years: overview. *Diabetes Care* 2014; 37 (1): 9-16.
- 4) Diabetes Canada Clinical Practice Guidelines Expert Committee; Berard LD, Siemens R, et al. Monitoring glycemic control. *Can J Diabetes* 2018; 42 Suppl 1: S47-53.
- 5) Ng SS, Kavanagh KL, McDonough MA, et al. Crystal structures of histone demethylase JMJD2A reveal basis for substrate specificity. *Nature* 2007; 448 (7149): 87-91.

- 6) Zhang Y, Wang H, Jia R, et al. Serum ferritin is associated with the presence of ischemic stroke among individuals with type 2 diabetes. *Heliyon* 2024; 10 (5) : e27898.
- 7) Kunutsor SK, Apekey TA, Walley J, et al. Ferritin levels and risk of type 2 diabetes mellitus: an updated systematic review and meta-analysis of prospective evidence. *Diabetes Metab Res Rev* 2013; 29 (4) : 308-18.
- 8) Qin Y, Huang Y, Li Y, et al. Association between systemic iron status and β -cell function and insulin sensitivity in patients with newly diagnosed type 2 diabetes. *Front Endocrinol (Lausanne)* 2023; 14: 1143919.