Diabetic patients: Maintain albumin level to avoid complications

The importance of albumin levels in regulation of glycation of plasma proteins is shown by a team led by Mahesh Kulkarni at CSIR-National Chemical Laboratory (www.ncl-india.org), Pune. The findings have been reported in the recent issue of Journal of Proteome Research published by the American Chemical Society.

Diabetes is characterized by increased levels of plasma glucose, which in turn modify blood plasma proteins by a non-enzymatic reaction called glycation. Protein glycation leads to formation of toxic molecules 'advanced glycation end products' (AGEs). Accumulation of AGEs has been found to be accelerated in diabetes and contribute to pathogenesis of diabetic complications.

Blood plasma proteins are the first to get modified as they are directly exposed to higher glucose concentrations and a number of them have been identified. Human serum albumin is one of most abundant plasma proteins and heavily glycated in diabetes. Albumin constitutes more than 50% of plasma proteins, and any variation in levels of albumin may change the stoichiometry of glycation of other plasma proteins glycation.

Albumin levels in plasma are affected by factors such as diet, lifestyle, inflammation, disease, drugs etc. In diabetes, albumin synthesis and secretion is decreased due to insulin deficiency. Therefore, it is expected that albumin levels decrease in diabetes and may affect plasma protein glycation and glycosylated haemoglobin (HbA1c) is a measure of high Glucose levels.

The researchers performed the study in three systems: 1) diabetic mice plasma 2) diabetic clinical plasma and 3) *in vitro* glycated plasma. In both mice and clinical experiments, increased plasma protein glycation was observed in plasma with low albumin than plasma with high albumin. Additionally, plasma albumin levels were negatively correlated with HbA1c.

In vitro experiment with different albumin levels confirmed that the variation in albumin levels is associated with plasma protein glycation, and albumin competes for glycation with other plasma proteins.

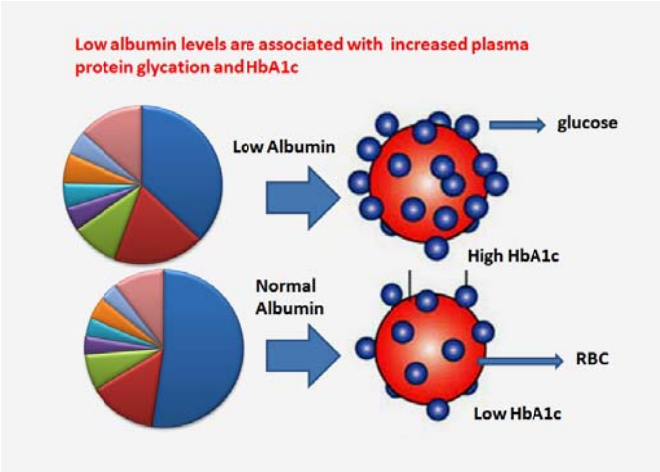
Previous studies have observed that patients with decreased albumin levels due to malnutrition were more prone to develop complications in diabetes. This study explained the basis of low albumin and higher risk of complications.

In conclusion, the major finding of this study was that low levels of albumin are associated with increased glycation of other plasma proteins such as HbA1c in diabetes.

This is the first study that shows the importance of albumin levels in regulation of glycation of HbA1c and other plasma proteins. Perhaps, maintaining near normal levels of albumin in diabetes could be one of the intervention strategies to protect plasma proteins from the adverse effects of glycation –a hypothesis that may be taken to clinical trials.

Dr. Ravi Sirdeshmukh, President, Proteomics Society India says that many plasma proteins have been shown to be prone to glycation in hyperglycemic conditions and resulting pathogenesis. Dr. Ravi describes this work of Kulkarni and his group as a very neat study carried out to explore the influence of albumin levels on the overall glycation of plasma proteins. The study exemplifies a neat execution of experiments from in vitro study to model animals to human clinical specimens and can be taken further for clinical exploitation.

This study was carried out in collaboration with Dr. Ramanamurthy Boppana, National Center for Cell Science and Dr. Kishore Shelgikar, Maharashtra Medical Research Society.



Top diagram: Albumin – 37%; Bottom diagram: Albumin - 52%

Further reading:

Bhonsle, H. S.; Korwar, A. M.; Kote, S. S.; Golegaonkar, S. B.; Chougale, A. D.; Shaik, M. L.; Dhande, N. L.; Giri, A. P.; Shelgikar, K. M.; Boppana, R.; and Kulkarni, M. J., Low plasma albumin levels are associated with increased plasma protein glycation and HbA1c in diabetes, *Journal of Proteome Research*, 2012, **11**, 1391-1396.

Bhonsle, H. S.; Singh, S. K.; Srivastava, G.; Boppana, R.; and Kulkarni, M. J., Albumin competitively inhibits glycation of less abundant proteins, Protein and Peptide Letters, 2008, **15**, 663−667.