



Relationship between proteolytic enzyme activity and oxidative stress in subjects with diabetes

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Dear Editor,

The manuscript entitled "Oxidative stress and proteolytic activity in erythrocytes of diabetic patients" by Varashree and Gopalakrishna (1) investigates the relationship between proteolytic enzyme activity and oxidative stress in subjects with diabetes. The results indicate that both erythrocyte malondialdehyde (MDA) levels and erythrocyte proteolytic activity were higher in diabetes patients than in control subjects (4.7 ± 1.7 nm/gHb v 3.3 ± 2.2 nm/gHb; $P = 0.001$ and 167.2 ± 648 nm/gHb v 27.9 ± 31.7 nm/gHb; $P = 0.001$, respectively).

The study is interesting and adds more information to the available literature on plasma biomarkers of oxidative stress. We would, however, highlight some areas of the study that seem to require clarification. First, in regard to the study sample, there is no mention of the type of diabetes that the subjects have. Judging by the ages of the patients, it seems likely that the majority would have Type 2 Diabetes Mellitus (T2DM). Additionally, no documen-

tation is made of the therapies used to control glucose and other baseline characteristics such as the duration of diabetes, BMI, presence of micro- or macrovascular complications, blood pressure, and other medications such as ACE inhibitors, statins, and aspirin, all of which could play a fundamental role in modifying the generation of reactive oxygen species (ROS). Moreover, no environmental factors such as smoking status, CHD status, or ethnicity are listed, all of which could contribute to increased ROS and cellular damage independently of diabetic status. The lack of information regarding insulin usage and dosage should be examined, especially given that reports suggest that insulin can simulate signal transduction pathways in erythrocytes that inhibit ATP release from the cell, thereby altering its energy output and ROS potential (2).

Within the study itself I question a few items. It is well documented that acute increases in blood glucose levels, such as postprandial glucose, have a significant, independent effect on ROS levels and ultimately on the pathogenesis of diabetic complications (3-5). The relative contribution of fasting and postprandial glucose levels to the value of HbA1c has been widely discussed (6-8), with the hypothesised ratio being 1:2. Therefore, it could be argued that measuring postprandial glucose or HbA1c as a marker for blood glucose levels would have been

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more useful than fasting blood glucose for the purpose of this investigation. It is also unclear from the methodology if blood haemoglobin levels were measured, as these would change regardless of whether the patient is suffering with anaemia.

Among the subjects with diabetes, fasting blood glucose was not correlated with either erythrocyte MDA levels or erythrocyte proteolytic activity, suggesting that both of these measures are independent of plasma glucose levels and hence not necessarily related to hyperglycaemia per se. Of further importance, erythrocyte MDA levels and erythrocyte proteolytic activity were not correlated with each other, suggesting that the increased levels of enzymatic activity are not necessarily related to increased levels of oxidative damage. Another factor that this study should consider is that proteolytic activity in human erythrocytes can vary depending on the age of the patient and the age of the cell itself (9,10).

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