

**Relationships Between Erythrocyte Osmotic Fragility and Vitamin C Nutriture in Adults With or Without Type 2 Diabetes**

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**Objectives:** Erythrocyte osmotic fragility is noted in Gulo<sup>-/-</sup> knockout mice unable to synthesize vitamin C, likely due to the decreased production of cytoskeletal  $\beta$ -spectrin, which affects cell deformability. Individuals with type 2 diabetes (T2D) commonly display marginal vitamin C nutriture, a consequence of reduced cellular uptake and recycling of dehydroascorbic acid. This cross-sectional study examined the relationships between vitamin C status and erythrocyte osmotic fragility in adults with or without T2D.

**Methods:** Participants did not report unresolved disease conditions or supplementation with vitamin C for the previous three months. T2D diagnosis occurred  $\geq 1$  year before study enrollment. Participants provided a fasting venous blood sample for erythrocyte osmotic fragility testing based on erythrocyte lysis with varying concentrations of sodium chloride. In addition, plasma was extracted and mixed with equal volume of 10% (w/v) metaphosphoric acid in 2 mmol/L disodium EDTA and centrifuged at 4°C. The supernatant was stored at  $-80^{\circ}\text{C}$

until analysis using isocratic reverse-phase UV-HPLC separation. All participants provided written informed consent and the study was approved by the local Institutional Review Board.

**Results:** Participant characteristics did not differ significantly between groups with the exception of age ( $P < 0.01$ ) and HbA1c ( $p = 0.002$ ). Data are presented for adults with T2D ( $n = 14$ ; 36% female;  $55.5 \pm 8.2$  y;  $31.5 \pm 9.0$  kg/m<sup>2</sup>; HbA1c:  $7.4 \pm 1.9\%$ ; plasma vitamin C:  $36.0 \pm 12.2$  mM) and adults without T2D ( $n = 16$ ; 69% female;  $38.7 \pm 13.5$  y;  $26.8 \pm 6.6$  kg/m<sup>2</sup>; A1c:  $5.4 \pm 0.3\%$ ; plasma vitamin C:  $34.8 \pm 10.9$  mM). Compared to adults with T2D, erythrocyte osmotic fragility was significantly elevated in adults without T2D at 0.35% saline ( $+4.4\%$ ,  $p = 0.021$ ). Vitamin C status did not impact erythrocyte osmotic fragility in adults with T2D; however, in adults without T2D, erythrocyte osmotic stability was linked to high vitamin C status at 0.35% saline ( $p = 0.054$  unadjusted and  $p = 0.022$  adjusted for age and gender).

**Conclusions:** In this small pilot trial, T2D was not related to increased erythrocyte osmotic fragility or marginal vitamin C status. However, vitamin C nutriture was directly linked to erythrocyte osmotic stability in adults without T2D.

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