

## ABSTRACT

### Glutathione Metabolism in Type 2 Diabetes

Fallon Kristie Lutchmansingh

Antioxidant glutathione (GSH) levels are decreased in type 2 diabetes (T2DM), this may be related to glycaemia. GSH concentration and rates of synthesis in persons with and without type 2 diabetes were compared and used to determine if any relationships are due to glycaemia. We recruited 8 non-diabetic persons, 7 persons with T2DM without complications as well as 9 persons with T2DM with diabetic microvascular complications. Fasting glucose, HbA1c, and lipids were measured. After an overnight fast, we infused H<sub>2</sub>-glycine for 8 hours. GSH kinetics was determined by liquid chromatography mass spectrometry. Compared to non-diabetic persons, persons with T2DM had lower GSH concentrations ( $0.90 \pm 0.15$  vs.  $0.35 \pm 0.08$  mmol/L;  $P=0.001$ ). Absolute synthesis rates (ASR) ( $1.03 \pm 0.19$  vs.  $0.50 \pm 0.17$  mmol/L/day;  $P = 0.07$ ) were lower in T2DM persons. Compared to non-diabetic persons, persons with complications had lower GSH Concentrations ( $0.22 \pm 0.04$  mmol/L;  $P < 0.001$ ) and ASR ( $0.31 \pm 0.06$  mmol/L/day;  $P < 0.03$ ). There were no significant differences in GSH levels between persons with T2DM and persons with complications ( $P$ -values  $> 0.1$ ). GSH concentration was not correlated with fasting glucose ( $r = -0.32$ ;  $P = 0.12$ ) Or HbA1c ( $r = -0.25$ ;  $P = 0.26$ ). The ASR was not correlated with glycaemia ( $P$ -

values  $> 0.17$ ). Microvascular complications significantly correlated with glutathione concentration ( $r = -0.51$ ;  $P = 0.012$ ) and absolute synthesis rates ( $r = -0.42$ ;  $P = 0.04$ ).

Persons with T2DM have glutathione deficiency especially those with diabetic Microvascular complications. This is probably due to reduced synthesis and increased irreversible utilization by non-glycaemic mechanisms.

**Keywords:** Fallon Kristie Lutchmansingh; glutathione, metabolism; Type 2 Diabetes (T2DM); glycaemia, stable isotope infusion; liquid chromatography mass spectrometry (LC-MS).